

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
13 September 2001 (13.09.2001)

PCT

(10) International Publication Number
WO 01/66690 A2

(51) International Patent Classification: C12N

(21) International Application Number: PCT/US01/07143

(22) International Filing Date: 5 March 2001 (05.03.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/187,107 6 March 2000 (06.03.2000) US
60/188,916 13 March 2000 (13.03.2000) US
60/236,874 3 October 2000 (03.10.2000) US
60/237,846 3 October 2000 (03.10.2000) US

(71) Applicants (for all designated States except US):
SMITHKLINE BEECHAM CORPORATION
[US/US]; One Franklin Plaza, Philadelphia, PA 19103
(US). SMITHKLINE BEECHAM P.L.C. [GB/GB]; New
Horizons Court, Great West Road, Brentford, Middlesex
TW8 9EP (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): AGARWAL,
Pankaj [IN/US]; 251 West DeKalb Pike, King of Prussia,

PA 19406 (US). MURDOCH, Paul, R. [GB/GB]; New
Frontiers Science Park South, Third Avenue, Harlow,
Essex CM19 5AW (GB). RIZVI, Safia, K. [PK/US];
4617 Pine Street, Philadelphia, PA 19143 (US). SMITH,
Randall, F. [US/US]; 4138 Presidential Drive, Lafayette
Hill, PA 19444 (US). XIANG, Zhaoying [CN/US]; 2413
Ridgeway, Fort Lee, NJ 07024 (US).

(74) Agents: GIMMI, Edward, R. et al.; SmithKline Beecham
Corporation, Corporate Intellectual Property, UW2220,
709 Swedeland Road, P.O. Box 1539, King of Prussia, PA
19406-0939 (US).

(81) Designated States (national): JP, US.

(84) Designated States (regional): European patent (AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,
NL, PT, SE, TR).

Published:

— without international search report and to be republished
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.



WO 01/66690 A2

(54) Title: NOVEL COMPOUNDS

(57) Abstract: Polypeptides and polynucleotides of the genes set forth in Table I and methods for producing such polypeptides by recombinant techniques are disclosed. Also disclosed are methods for utilizing polypeptides and polynucleotides of the genes set forth in Table I in diagnostic assays.

Novel Compounds

Field of Invention

5 This invention relates to newly identified polypeptides and polynucleotides encoding such polypeptides, to their use in diagnosis and in identifying compounds that may be agonists, antagonists that are potentially useful in therapy, and to production of such polypeptides and polynucleotides. The polynucleotides and polypeptides of the present invention also relate to proteins with signal sequences which allow them to be secreted
10 extracellularly or membrane-associated (hereinafter often referred collectively as secreted proteins or secreted polypeptides).

Background of the Invention

 The drug discovery process is currently undergoing a fundamental revolution as it
15 embraces "functional genomics", that is, high throughput genome- or gene-based biology. This approach as a means to identify genes and gene products as therapeutic targets is rapidly superseding earlier approaches based on "positional cloning". A phenotype, that is a biological function or genetic disease, would be identified and this would then be tracked back to the responsible gene, based on its genetic map position.

20 Functional genomics relies heavily on high-throughput DNA sequencing technologies and the various tools of bioinformatics to identify gene sequences of potential interest from the many molecular biology databases now available. There is a continuing need to identify and characterise further genes and their related polypeptides/proteins, as targets for drug discovery.

25 Proteins and polypeptides that are naturally secreted into blood, lymph and other body fluids, or secreted into the cellular membrane are of primary interest for pharmaceutical research and development. The reason for this interest is the relative ease to target protein therapeutics into their place of action (body fluids or the cellular membrane). The natural pathway for protein secretion into extracellular space is the endoplasmic reticulum in
30 eukaryotes and the inner membrane in prokaryotes (Palade, 1975, Science, 189, 347; Milstein, Brownlee, Harrison, and Mathews, 1972, Nature New Biol., 239, 117; Blobel, and Dobberstein, 1975, J. Cell. Biol., 67, 835). On the other hand, there is no known natural pathway for exporting a protein from the exterior of the cells into the cytosol (with the exception of pinocytosis, a mechanism of snake venom toxin intrusion into cells). Therefore
35 targeting protein therapeutics into cells poses extreme difficulties.

 The secreted and membrane-associated proteins include but are not limited to

all peptide hormones and their receptors (including but not limited to insulin, growth hormones, chemokines, cytokines, neuropeptides, integrins, kallikreins, lamins, melanins, natriuretic hormones, neuropsin, neurotrophins, pituitary hormones, pleiotropins, prostaglandins, secretogranins, selectins, thromboglobulins, thymosins),
5 the breast and colon cancer gene products, leptin, the obesity gene protein and its receptors, serum albumin, superoxide dismutase, spliceosome proteins, 7TM (transmembrane) proteins also called as G-protein coupled receptors, immunoglobulins, several families of serine proteinases (including but not limited to proteins of the blood coagulation cascade, digestive enzymes), deoxyribonuclease I,
10 etc.

Therapeutics based on secreted or membrane-associated proteins approved by FDA or foreign agencies include but are not limited to insulin, glucagon, growth hormone, chorionic gonadotropin, follicle stimulating hormone, luteinizing hormone, calcitonin, adrenocorticotrophic hormone (ACTH), vasopressin, interleukines,
15 interferones, immunoglobulins, lactoferrin (diverse products marketed by several companies), tissue-type plasminogen activator (Alteplase by Genentech), hyaluronidase (Wydase by Wyeth-Ayerst), dornase alpha (Pulmozyme by Genentech), Chymodiactin (chymopapain by Knoll), alglucerase (Ceredase by Genzyme), streptokinase (Kabikinase by Pharmacia) (Streptase by Astra), etc. This
20 indicates that secreted and membrane-associated proteins have an established, proven history as therapeutic targets. Clearly, there is a need for identification and characterization of further secreted and membrane-associated proteins which can play a role in preventing, ameliorating or correcting dysfunction or disease, including but not limited to diabetes, breast-, prostate-, colon cancer and other malignant tumors,
25 hyper- and hypotension, obesity, bulimia, anorexia, growth abnormalities, asthma, manic depression, dementia, delirium, mental retardation, Huntington's disease, Tourette's syndrome, schizophrenia, growth, mental or sexual development disorders, and dysfunctions of the blood cascade system including those leading to stroke. The proteins of the present invention which include the signal sequences are also useful to
30 further elucidate the mechanism of protein transport which at present is not entirely understood, and thus can be used as research tools.

Summary of the Invention

The present invention relates to particular polypeptides and polynucleotides of the
35 genes set forth in Table I, including recombinant materials and methods for their production. Such polypeptides and polynucleotides are of interest in relation to methods of treatment of

certain diseases, including, but not limited to, the diseases set forth in Tables III and V, hereinafter referred to as "diseases of the invention". In a further aspect, the invention relates to methods for identifying agonists and antagonists (*e.g.*, inhibitors) using the materials provided by the invention, and treating conditions associated with imbalance of polypeptides and/or polynucleotides of the genes set forth in Table I with the identified compounds. In still a further aspect, the invention relates to diagnostic assays for detecting diseases associated with inappropriate activity or levels the genes set forth in Table I. Another aspect of the invention concerns a polynucleotide comprising any of the nucleotide sequences set forth in the Sequence Listing and a polypeptide comprising a polypeptide encoded by the nucleotide sequence. In another aspect, the invention relates to a polypeptide comprising any of the polypeptide sequences set forth in the Sequence Listing and recombinant materials and methods for their production. Another aspect of the invention relates to methods for using such polypeptides and polynucleotides. Such uses include the treatment of diseases, abnormalities and disorders (hereinafter simply referred to as diseases) caused by abnormal expression, production, function and or metabolism of the genes of this invention, and such diseases are readily apparent by those skilled in the art from the homology to other proteins disclosed for each attached sequence. In still another aspect, the invention relates to methods to identify agonists and antagonists using the materials provided by the invention, and treating conditions associated with the imbalance with the identified compounds. Yet another aspect of the invention relates to diagnostic assays for detecting diseases associated with inappropriate activity or levels of the secreted proteins of the present invention.

Description of the Invention

In a first aspect, the present invention relates to polypeptides the genes set forth in Table I. Such polypeptides include:

- (a) an isolated polypeptide encoded by a polynucleotide comprising a sequence set forth in the Sequence Listing, herein when referring to polynucleotides or polypeptides of the Sequence Listing, a reference is also made to the Sequence Listing referred to in the Sequence Listing;
- (b) an isolated polypeptide comprising a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;
- (c) an isolated polypeptide comprising a polypeptide sequence set forth in the Sequence Listing;
- (d) an isolated polypeptide having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;

(e) a polypeptide sequence set forth in the Sequence Listing; and
(f) an isolated polypeptide having or comprising a polypeptide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polypeptide sequence set forth in the Sequence Listing;

5 (g) fragments and variants of such polypeptides in (a) to (f).

Polypeptides of the present invention are believed to be members of the gene families set forth in Table II. They are therefore of therapeutic and diagnostic interest for the reasons set forth in Tables III and V. The biological properties of the polypeptides and polynucleotides of the genes set forth in Table I are hereinafter referred to as "the biological activity" of

10 polypeptides and polynucleotides of the genes set forth in Table I. Preferably, a polypeptide of the present invention exhibits at least one biological activity of the genes set forth in Table I.

Polypeptides of the present invention also include variants of the aforementioned polypeptides, including all allelic forms and splice variants. Such polypeptides vary from the reference polypeptide by insertions, deletions, and substitutions that may be conservative or
15 non-conservative, or any combination thereof. Particularly preferred variants are those in which several, for instance from 50 to 30, from 30 to 20, from 20 to 10, from 10 to 5, from 5 to 3, from 3 to 2, from 2 to 1 or 1 amino acids are inserted, substituted, or deleted, in any combination.

20 Preferred fragments of polypeptides of the present invention include an isolated polypeptide comprising an amino acid sequence having at least 30, 50 or 100 contiguous amino acids from an amino acid sequence set forth in the Sequence Listing, or an isolated polypeptide comprising an amino acid sequence having at least 30, 50 or 100 contiguous amino acids truncated or deleted from an amino acid sequence set forth in the Sequence
25 Listing. Preferred fragments are biologically active fragments that mediate the biological activity of polypeptides and polynucleotides of the genes set forth in Table I, including those with a similar activity or an improved activity, or with a decreased undesirable activity. Also preferred are those fragments that are antigenic or immunogenic in an animal, especially in a human.

30 Fragments of a polypeptide of the invention may be employed for producing the corresponding full-length polypeptide by peptide synthesis; therefore, these variants may be employed as intermediates for producing the full-length polypeptides of the invention. A polypeptide of the present invention may be in the form of the "mature" protein or may be a part of a larger protein such as a precursor or a fusion protein. It is often advantageous to
35 include an additional amino acid sequence that contains secretory or leader sequences, pro-

sequences, sequences that aid in purification, for instance multiple histidine residues, or an additional sequence for stability during recombinant production.

Polypeptides of the present invention can be prepared in any suitable manner, for instance by isolation from naturally occurring sources, from genetically engineered host cells comprising expression systems (*vide infra*) or by chemical synthesis, using for instance automated peptide synthesizers, or a combination of such methods. Means for preparing such polypeptides are well understood in the art.

In a further aspect, the present invention relates to polynucleotides of the genes set forth in Table I. Such polynucleotides include:

- 10 (a) an isolated polynucleotide comprising a polynucleotide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide sequence set forth in the Sequence Listing;
- (b) an isolated polynucleotide comprising a polynucleotide set forth in the Sequence Listing;
- (c) an isolated polynucleotide having at least 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide set forth in the Sequence Listing;
- 15 (d) an isolated polynucleotide set forth in the Sequence Listing;
- (e) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;
- 20 (f) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide set forth in the Sequence Listing;
- (g) an isolated polynucleotide having a polynucleotide sequence encoding a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;
- 25 (h) an isolated polynucleotide encoding a polypeptide set forth in the Sequence Listing;
- (i) an isolated polynucleotide having or comprising a polynucleotide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polynucleotide sequence set forth in the Sequence Listing;
- (j) an isolated polynucleotide having or comprising a polynucleotide sequence encoding a polypeptide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polypeptide sequence set forth in the Sequence Listing; and
- 30 polynucleotides that are fragments and variants of the above mentioned polynucleotides or that are complementary to above mentioned polynucleotides, over the entire length thereof.

Preferred fragments of polynucleotides of the present invention include an isolated polynucleotide comprising a nucleotide sequence having at least 15, 30, 50 or 100

contiguous nucleotides from a sequence set forth in the Sequence Listing, or an isolated polynucleotide comprising a sequence having at least 30, 50 or 100 contiguous nucleotides truncated or deleted from a sequence set forth in the Sequence Listing.

Preferred variants of polynucleotides of the present invention include splice variants, allelic variants, and polymorphisms, including polynucleotides having one or more single nucleotide polymorphisms (SNPs).

Polynucleotides of the present invention also include polynucleotides encoding polypeptide variants that comprise an amino acid sequence set forth in the Sequence Listing and in which several, for instance from 50 to 30, from 30 to 20, from 20 to 10, from 10 to 5, from 5 to 3, from 3 to 2, from 2 to 1 or 1 amino acid residues are substituted, deleted or added, in any combination.

In a further aspect, the present invention provides polynucleotides that are RNA transcripts of the DNA sequences of the present invention. Accordingly, there is provided an RNA polynucleotide that:

- (a) comprises an RNA transcript of the DNA sequence encoding a polypeptide set forth in the Sequence Listing;
- (b) is a RNA transcript of a DNA sequence encoding a polypeptide set forth in the Sequence Listing;
- (c) comprises an RNA transcript of a DNA sequence set forth in the Sequence Listing; or
- (d) is a RNA transcript of a DNA sequence set forth in the Sequence Listing; and RNA polynucleotides that are complementary thereto.

The polynucleotide sequences set forth in the Sequence Listing show homology with the polynucleotide sequences set forth in Table II. A polynucleotide sequence set forth in the Sequence Listing is a cDNA sequence that encodes a polypeptide set forth in the Sequence Listing. A polynucleotide sequence encoding a polypeptide set forth in the Sequence Listing may be identical to a polypeptide encoding a sequence set forth in the Sequence Listing or it may be a sequence other than a sequence set forth in the Sequence Listing, which, as a result of the redundancy (degeneracy) of the genetic code, also encodes a polypeptide set forth in the Sequence Listing. A polypeptide of a sequence set forth in the Sequence Listing is related to other proteins of the gene families set forth in Table II, having homology and/or structural similarity with the polypeptides set forth in Table II. Preferred polypeptides and polynucleotides of the present invention are expected to have, *inter alia*, similar biological functions/properties to their homologous polypeptides and polynucleotides. Furthermore,

preferred polypeptides and polynucleotides of the present invention have at least one activity of the genes set forth in Table I.

Polynucleotides of the present invention may be obtained using standard cloning and screening techniques from a cDNA library derived from mRNA from the tissues set forth in Table IV (see for instance, Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)).

Polynucleotides of the invention can also be obtained from natural sources such as genomic DNA libraries or can be synthesized using well known and commercially available techniques.

When polynucleotides of the present invention are used for the recombinant production of polypeptides of the present invention, the polynucleotide may include the coding sequence for the mature polypeptide, by itself, or the coding sequence for the mature polypeptide in reading frame with other coding sequences, such as those encoding a leader or secretory sequence, a pre-, or pro- or prepro- protein sequence, or other fusion peptide portions. For example, a marker sequence that facilitates purification of the fused polypeptide can be encoded. In certain preferred embodiments of this aspect of the invention, the marker sequence is a hexa-histidine peptide, as provided in the pQE vector (Qiagen, Inc.) and described in Gentz *et al.*, Proc Natl Acad Sci USA (1989) 86:821-824, or is an HA tag. A polynucleotide may also contain non-coding 5' and 3' sequences, such as transcribed, non-translated sequences, splicing and polyadenylation signals, ribosome binding sites and sequences that stabilize mRNA.

Polynucleotides that are identical, or have sufficient identity to a polynucleotide sequence set forth in the Sequence Listing, may be used as hybridization probes for cDNA and genomic DNA or as primers for a nucleic acid amplification reaction (for instance, PCR).

Such probes and primers may be used to isolate full-length cDNAs and genomic clones encoding polypeptides of the present invention and to isolate cDNA and genomic clones of other genes (including genes encoding paralogs from human sources and orthologs and paralogs from species other than) that have a high sequence similarity to sequences set forth in the Sequence Listing, typically at least 95% identity. Preferred probes and primers will generally comprise at least 15 nucleotides, preferably, at least 30 nucleotides and may have at least 50, if not at least 100 nucleotides. Particularly preferred probes will have between 30 and 50 nucleotides. Particularly preferred primers will have between 20 and 25 nucleotides.

A polynucleotide encoding a polypeptide of the present invention, including homologs from species other than , may be obtained by a process comprising the steps of screening a library under stringent hybridization conditions with a labeled probe having a

sequence set forth in the Sequence Listing or a fragment thereof, preferably of at least 15 nucleotides; and isolating full-length cDNA and genomic clones containing the polynucleotide sequence set forth in the Sequence Listing. Such hybridization techniques are well known to the skilled artisan. Preferred stringent hybridization conditions include

5 overnight incubation at 42°C in a solution comprising: 50% formamide, 5xSSC (150mM NaCl, 15mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10 % dextran sulfate, and 20 microgram/ml denatured, sheared salmon sperm DNA; followed

10 by washing the filters in 0.1x SSC at about 65°C. Thus the present invention also includes isolated polynucleotides, preferably with a nucleotide sequence of at least 100, obtained by screening a library under stringent hybridization conditions with a labeled probe having the sequence set forth in the Sequence Listing or a fragment thereof, preferably of at least 15 nucleotides.

The skilled artisan will appreciate that, in many cases, an isolated cDNA sequence will be incomplete, in that the region coding for the polypeptide does not extend all the way

15 through to the 5' terminus. This is a consequence of reverse transcriptase, an enzyme with inherently low "processivity" (a measure of the ability of the enzyme to remain attached to the template during the polymerisation reaction), failing to complete a DNA copy of the mRNA template during first strand cDNA synthesis.

There are several methods available and well known to those skilled in the art to

20 obtain full-length cDNAs, or extend short cDNAs, for example those based on the method of Rapid Amplification of cDNA ends (RACE) (see, for example, Frohman et al., Proc Nat Acad Sci USA 85, 8998-9002, 1988). Recent modifications of the technique, exemplified by the Marathon (trade mark) technology (Clontech Laboratories Inc.) for example, have significantly simplified the search for longer cDNAs. In the Marathon (trade mark)

25 technology, cDNAs have been prepared from mRNA extracted from a chosen tissue and an 'adaptor' sequence ligated onto each end. Nucleic acid amplification (PCR) is then carried out to amplify the "missing" 5' end of the cDNA using a combination of gene specific and adaptor specific oligonucleotide primers. The PCR reaction is then repeated using 'nested' primers, that is, primers designed to anneal within the amplified product (typically an adapter specific

30 primer that anneals further 3' in the adaptor sequence and a gene specific primer that anneals further 5' in the known gene sequence). The products of this reaction can then be analyzed by DNA sequencing and a full-length cDNA constructed either by joining the product directly to the existing cDNA to give a complete sequence, or carrying out a separate full-length PCR using the new sequence information for the design of the 5' primer.

Recombinant polypeptides of the present invention may be prepared by processes well known in the art from genetically engineered host cells comprising expression systems. Accordingly, in a further aspect, the present invention relates to expression systems comprising a polynucleotide or polynucleotides of the present invention, to host cells which
5 are genetically engineered with such expression systems and to the production of polypeptides of the invention by recombinant techniques. Cell-free translation systems can also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention.

For recombinant production, host cells can be genetically engineered to incorporate
10 expression systems or portions thereof for polynucleotides of the present invention. Polynucleotides may be introduced into host cells by methods described in many standard laboratory manuals, such as Davis et al., Basic Methods in Molecular Biology (1986) and Sambrook *et al. (ibid)*. Preferred methods of introducing polynucleotides into host cells include, for instance, calcium phosphate transfection, DEAE-dextran mediated transfection,
15 transfection, micro-injection, cationic lipid-mediated transfection, electroporation, transduction, scrape loading, ballistic introduction or infection.

Representative examples of appropriate hosts include bacterial cells, such as *Streptococci*, *Staphylococci*, *E. coli*, *Streptomyces* and *Bacillus subtilis* cells; fungal cells, such as yeast cells and *Aspergillus* cells; insect cells such as *Drosophila* S2 and *Spodoptera*
20 Sf9 cells; animal cells such as CHO, COS, HeLa, C127, 3T3, BHK, HEK 293 and Bowes melanoma cells; and plant cells.

A great variety of expression systems can be used, for instance, chromosomal, episomal and virus-derived systems, *e.g.*, vectors derived from bacterial plasmids, from bacteriophage, from transposons, from yeast episomes, from insertion elements, from yeast
25 chromosomal elements, from viruses such as baculoviruses, papova viruses, such as SV40, vaccinia viruses, adenoviruses, fowl pox viruses, pseudorabies viruses and retroviruses, and vectors derived from combinations thereof, such as those derived from plasmid and bacteriophage genetic elements, such as cosmids and phagemids. The expression systems may contain control regions that regulate as well as engender expression. Generally, any
30 system or vector that is able to maintain, propagate or express a polynucleotide to produce a polypeptide in a host may be used. The appropriate polynucleotide sequence may be inserted into an expression system by any of a variety of well-known and routine techniques, such as, for example, those set forth in Sambrook *et al., (ibid)*. Appropriate secretion signals may be incorporated into the desired polypeptide to allow secretion of the translated protein into the

lumen of the endoplasmic reticulum, the periplasmic space or the extracellular environment. These signals may be endogenous to the polypeptide or they may be heterologous signals.

If a polypeptide of the present invention is to be expressed for use in screening assays, it is generally preferred that the polypeptide be produced at the surface of the cell. In this event, the cells may be harvested prior to use in the screening assay. If the polypeptide is secreted into the medium, the medium can be recovered in order to recover and purify the polypeptide. If produced intracellularly, the cells must first be lysed before the polypeptide is recovered.

Polypeptides of the present invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography is employed for purification. Well known techniques for refolding proteins may be employed to regenerate active conformation when the polypeptide is denatured during intracellular synthesis, isolation and/or purification.

Polynucleotides of the present invention may be used as diagnostic reagents, through detecting mutations in the associated gene. Detection of a mutated form of a gene is characterized by the polynucleotides set forth in the Sequence Listing in the cDNA or genomic sequence and which is associated with a dysfunction. Will provide a diagnostic tool that can add to, or define, a diagnosis of a disease, or susceptibility to a disease, which results from under-expression, over-expression or altered spatial or temporal expression of the gene. Individuals carrying mutations in the gene may be detected at the DNA level by a variety of techniques well known in the art.

Nucleic acids for diagnosis may be obtained from a subject's cells, such as from blood, urine, saliva, tissue biopsy or autopsy material. The genomic DNA may be used directly for detection or it may be amplified enzymatically by using PCR, preferably RT-PCR, or other amplification techniques prior to analysis. RNA or cDNA may also be used in similar fashion. Deletions and insertions can be detected by a change in size of the amplified product in comparison to the normal genotype. Point mutations can be identified by hybridizing amplified DNA to labeled nucleotide sequences of the genes set forth in Table I. Perfectly matched sequences can be distinguished from mismatched duplexes by RNase digestion or by differences in melting temperatures. DNA sequence difference may also be detected by alterations in the electrophoretic mobility of DNA fragments in gels, with or without denaturing agents, or by direct DNA sequencing (see, for instance, Myers *et al.*,

Science (1985) 230:1242). Sequence changes at specific locations may also be revealed by nuclease protection assays, such as RNase and S1 protection or the chemical cleavage method (see Cotton *et al.*, Proc Natl Acad Sci USA (1985) 85: 4397-4401).

5 An array of oligonucleotides probes comprising polynucleotide sequences or fragments thereof of the genes set forth in Table I can be constructed to conduct efficient screening of *e.g.*, genetic mutations. Such arrays are preferably high density arrays or grids. Array technology methods are well known and have general applicability and can be used to address a variety of questions in molecular genetics including gene expression, genetic linkage, and genetic variability, see, for example, M. Chee *et al.*, Science, 274, 610-613
10 (1996) and other references cited therein.

Detection of abnormally decreased or increased levels of polypeptide or mRNA expression may also be used for diagnosing or determining susceptibility of a subject to a disease of the invention. Decreased or increased expression can be measured at the RNA level using any of the methods well known in the art for the quantitation of polynucleotides, such as, for
15 example, nucleic acid amplification, for instance PCR, RT-PCR, RNase protection, Northern blotting and other hybridization methods. Assay techniques that can be used to determine levels of a protein, such as a polypeptide of the present invention, in a sample derived from a host are well-known to those of skill in the art. Such assay methods include radio-immunoassays, competitive-binding assays, Western Blot analysis and ELISA assays.

20 Thus in another aspect, the present invention relates to a diagnostic kit comprising:
(a) a polynucleotide of the present invention, preferably the nucleotide sequence set forth in the Sequence Listing, or a fragment or an RNA transcript thereof;
(b) a nucleotide sequence complementary to that of (a);
(c) a polypeptide of the present invention, preferably the polypeptide set forth in the Sequence
25 Listing or a fragment thereof; or
(d) an antibody to a polypeptide of the present invention, preferably to the polypeptide set forth in the Sequence Listing.

It will be appreciated that in any such kit, (a), (b), (c) or (d) may comprise a substantial component. Such a kit will be of use in diagnosing a disease or susceptibility to a
30 disease, particularly diseases of the invention, amongst others.

The polynucleotide sequences of the present invention are valuable for chromosome localisation studies. The sequences set forth in the Sequence Listing are specifically targeted to, and can hybridize with, a particular location on an individual human chromosome. The mapping of relevant sequences to chromosomes according to the present invention is an
35 important first step in correlating those sequences with gene associated disease. Once a

sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found in, for example, V. McKusick, Mendelian Inheritance in Man (available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and diseases that have been mapped to the same chromosomal region are then identified through linkage analysis (co-inheritance of physically adjacent genes). Precise human chromosomal localisations for a genomic sequence (gene fragment etc.) can be determined using Radiation Hybrid (RH) Mapping (Walter, M. Spillett, D., Thomas, P., Weissenbach, J., and Goodfellow, P., (1994) A method for constructing radiation hybrid maps of whole genomes, *Nature Genetics* 7, 22-28). A number of RH panels are available from Research Genetics (Huntsville, AL, USA) e.g. the GeneBridge4 RH panel (*Hum Mol Genet* 1996 Mar;5(3):339-46 A radiation hybrid map of the human genome. Gyapay G, Schmitt K, Fizames C, Jones H, Vega-Czarny N, Spillett D, Muselet D, Prud'Homme JF, Dib C, Auffray C, Morissette J, Weissenbach J, Goodfellow PN). To determine the chromosomal location of a gene using this panel, 93 PCRs are performed using primers designed from the gene of interest on RH DNAs. Each of these DNAs contains random human genomic fragments maintained in a hamster background (human / hamster hybrid cell lines). These PCRs result in 93 scores indicating the presence or absence of the PCR product of the gene of interest. These scores are compared with scores created using PCR products from genomic sequences of known location. This comparison is conducted at <http://www.genome.wi.mit.edu/>.

The polynucleotide sequences of the present invention are also valuable tools for tissue expression studies. Such studies allow the determination of expression patterns of polynucleotides of the present invention which may give an indication as to the expression patterns of the encoded polypeptides in tissues, by detecting the mRNAs that encode them. The techniques used are well known in the art and include in situ hybridization techniques to clones arrayed on a grid, such as cDNA microarray hybridization (Schena *et al*, *Science*, 270, 467-470, 1995 and Shalon *et al*, *Genome Res*, 6, 639-645, 1996) and nucleotide amplification techniques such as PCR. A preferred method uses the TAQMAN (Trade mark) technology available from Perkin Elmer. Results from these studies can provide an indication of the normal function of the polypeptide in the organism. In addition, comparative studies of the normal expression pattern of mRNAs with that of mRNAs encoded by an alternative form of the same gene (for example, one having an alteration in polypeptide coding potential or a regulatory mutation) can provide valuable insights into the role of the polypeptides of the present invention, or that of inappropriate expression thereof in disease. Such inappropriate expression may be of a temporal, spatial or simply quantitative nature.

A further aspect of the present invention relates to antibodies. The polypeptides of the invention or their fragments, or cells expressing them, can be used as immunogens to produce antibodies that are immunospecific for polypeptides of the present invention. The term "immunospecific" means that the antibodies have substantially greater affinity for the polypeptides of the invention than their affinity for other related polypeptides in the prior art.

Antibodies generated against polypeptides of the present invention may be obtained by administering the polypeptides or epitope-bearing fragments, or cells to an animal, preferably a non-human animal, using routine protocols. For preparation of monoclonal antibodies, any technique which provides antibodies produced by continuous cell line cultures can be used. Examples include the hybridoma technique (Kohler, G. and Milstein, C., *Nature* (1975) 256:495-497), the trioma technique, the human B-cell hybridoma technique (Kozbor *et al.*, *Immunology Today* (1983) 4:72) and the EBV-hybridoma technique (Cole *et al.*, *Monoclonal Antibodies and Cancer Therapy*, 77-96, Alan R. Liss, Inc., 1985).

Techniques for the production of single chain antibodies, such as those described in U.S. Patent No. 4,946,778, can also be adapted to produce single chain antibodies to polypeptides of this invention. Also, transgenic mice, or other organisms, including other mammals, may be used to express humanized antibodies.

The above-described antibodies may be employed to isolate or to identify clones expressing the polypeptide or to purify the polypeptides by affinity chromatography. Antibodies against polypeptides of the present invention may also be employed to treat diseases of the invention, amongst others.

Polypeptides and polynucleotides of the present invention may also be used as vaccines. Accordingly, in a further aspect, the present invention relates to a method for inducing an immunological response in a mammal that comprises inoculating the mammal with a polypeptide of the present invention, adequate to produce antibody and/or T cell immune response, including, for example, cytokine-producing T cells or cytotoxic T cells, to protect said animal from disease, whether that disease is already established within the individual or not. An immunological response in a mammal may also be induced by a method comprises delivering a polypeptide of the present invention *via* a vector directing expression of the polynucleotide and coding for the polypeptide *in vivo* in order to induce such an immunological response to produce antibody to protect said animal from diseases of the invention. One way of administering the vector is by accelerating it into the desired cells as a coating on particles or otherwise. Such nucleic acid vector may comprise DNA, RNA, a modified nucleic acid, or a DNA/RNA hybrid. For use a vaccine, a polypeptide or a nucleic acid vector will be normally provided as a vaccine formulation (composition). The

formulation may further comprise a suitable carrier. Since a polypeptide may be broken down in the stomach, it is preferably administered parenterally (for instance, subcutaneous, intra-muscular, intravenous, or intra-dermal injection). Formulations suitable for parenteral administration include aqueous and non-aqueous sterile injection solutions that may contain
5 anti-oxidants, buffers, bacteriostats and solutes that render the formulation isotonic with the blood of the recipient; and aqueous and non-aqueous sterile suspensions that may include suspending agents or thickening agents. The formulations may be presented in unit-dose or multi-dose containers, for example, sealed ampoules and vials and may be stored in a freeze-dried condition requiring only the addition of the sterile liquid carrier immediately prior to
10 use. The vaccine formulation may also include adjuvant systems for enhancing the immunogenicity of the formulation, such as oil-in water systems and other systems known in the art. The dosage will depend on the specific activity of the vaccine and can be readily determined by routine experimentation.

Polypeptides of the present invention have one or more biological functions that are
15 of relevance in one or more disease states, in particular the diseases of the invention hereinbefore mentioned. It is therefore useful to identify compounds that stimulate or inhibit the function or level of the polypeptide. Accordingly, in a further aspect, the present invention provides for a method of screening compounds to identify those that stimulate or inhibit the function or level of the polypeptide. Such methods identify agonists or antagonists
20 that may be employed for therapeutic and prophylactic purposes for such diseases of the invention as hereinbefore mentioned. Compounds may be identified from a variety of sources, for example, cells, cell-free preparations, chemical libraries, collections of chemical compounds, and natural product mixtures. Such agonists or antagonists so-identified may be natural or modified substrates, ligands, receptors, enzymes, etc., as the case may be, of the
25 polypeptide; a structural or functional mimetic thereof (see Coligan *et al.*, Current Protocols in Immunology 1(2):Chapter 5 (1991)) or a small molecule. Such small molecules preferably have a molecular weight below 2,000 daltons, more preferably between 300 and 1,000 daltons, and most preferably between 400 and 700 daltons. It is preferred that these small molecules are organic molecules.

30 The screening method may simply measure the binding of a candidate compound to the polypeptide, or to cells or membranes bearing the polypeptide, or a fusion protein thereof, by means of a label directly or indirectly associated with the candidate compound. Alternatively, the screening method may involve measuring or detecting (qualitatively or quantitatively) the competitive binding of a candidate compound to the polypeptide against a
35 labeled competitor (*e.g.* agonist or antagonist). Further, these screening methods may test

whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide, using detection systems appropriate to the cells bearing the polypeptide. Inhibitors of activation are generally assayed in the presence of a known agonist and the effect on activation by the agonist by the presence of the candidate compound is observed.

5 Further, the screening methods may simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide of the present invention, to form a mixture, measuring an activity of the genes set forth in Table I in the mixture, and comparing activity of the mixture of the genes set forth in Table I to a control mixture which contains no candidate compound.

10 Polypeptides of the present invention may be employed in conventional low capacity screening methods and also in high-throughput screening (HTS) formats. Such HTS formats include not only the well-established use of 96- and, more recently, 384-well micotiter plates but also emerging methods such as the nanowell method described by Schullek et al, *Anal Biochem.*, 246, 20-29, (1997).

15 Fusion proteins, such as those made from Fc portion and polypeptide of the genes set forth in Table I, as hereinbefore described, can also be used for high-throughput screening assays to identify antagonists for the polypeptide of the present invention (see D. Bennett *et al.*, *J Mol Recognition*, 8:52-58 (1995); and K. Johanson *et al.*, *J Biol Chem*, 270(16):9459-9471 (1995)).

20 The polynucleotides, polypeptides and antibodies to the polypeptide of the present invention may also be used to configure screening methods for detecting the effect of added compounds on the production of mRNA and polypeptide in cells. For example, an ELISA assay may be constructed for measuring secreted or cell associated levels of polypeptide using monoclonal and polyclonal antibodies by standard methods known in the art. This can be
25 used to discover agents that may inhibit or enhance the production of polypeptide (also called antagonist or agonist, respectively) from suitably manipulated cells or tissues.

A polypeptide of the present invention may be used to identify membrane bound or soluble receptors, if any, through standard receptor binding techniques known in the art. These include, but are not limited to, ligand binding and crosslinking assays in which the
30 polypeptide is labeled with a radioactive isotope (for instance, ^{125}I), chemically modified (for instance, biotinylated), or fused to a peptide sequence suitable for detection or purification, and incubated with a source of the putative receptor (cells, cell membranes, cell supernatants, tissue extracts, bodily fluids). Other methods include biophysical techniques such as surface plasmon resonance and spectroscopy. These screening methods may also be used to identify
35 agonists and antagonists of the polypeptide that compete with the binding of the polypeptide

to its receptors, if any. Standard methods for conducting such assays are well understood in the art.

Examples of antagonists of polypeptides of the present invention include antibodies or, in some cases, oligonucleotides or proteins that are closely related to the ligands, substrates, receptors, enzymes, etc., as the case may be, of the polypeptide, *e.g.*, a fragment of the ligands, substrates, receptors, enzymes, etc.; or a small molecule that bind to the polypeptide of the present invention but do not elicit a response, so that the activity of the polypeptide is prevented.

Screening methods may also involve the use of transgenic technology and the genes set forth in Table I. The art of constructing transgenic animals is well established. For example, the genes set forth in Table I may be introduced through microinjection into the male pronucleus of fertilized oocytes, retroviral transfer into pre- or post-implantation embryos, or injection of genetically modified, such as by electroporation, embryonic stem cells into host blastocysts. Particularly useful transgenic animals are so-called "knock-in" animals in which an animal gene is replaced by the human equivalent within the genome of that animal. Knock-in transgenic animals are useful in the drug discovery process, for target validation, where the compound is specific for the human target. Other useful transgenic animals are so-called "knock-out" animals in which the expression of the animal ortholog of a polypeptide of the present invention and encoded by an endogenous DNA sequence in a cell is partially or completely annulled. The gene knock-out may be targeted to specific cells or tissues, may occur only in certain cells or tissues as a consequence of the limitations of the technology, or may occur in all, or substantially all, cells in the animal. Transgenic animal technology also offers a whole animal expression-cloning system in which introduced genes are expressed to give large amounts of polypeptides of the present invention

Screening kits for use in the above described methods form a further aspect of the present invention. Such screening kits comprise:

- (a) a polypeptide of the present invention;
 - (b) a recombinant cell expressing a polypeptide of the present invention;
 - (c) a cell membrane expressing a polypeptide of the present invention; or
 - (d) an antibody to a polypeptide of the present invention;
- which polypeptide is preferably that set forth in the Sequence Listing.

It will be appreciated that in any such kit, (a), (b), (c) or (d) may comprise a substantial component.

Glossary

The following definitions are provided to facilitate understanding of certain terms used frequently hereinbefore.

"Antibodies" as used herein includes polyclonal and monoclonal antibodies, chimeric, single chain, and humanized antibodies, as well as Fab fragments, including the products of an

5 Fab or other immunoglobulin expression library.

"Isolated" means altered "by the hand of man" from its natural state, *i.e.*, if it occurs in nature, it has been changed or removed from its original environment, or both. For example, a polynucleotide or a polypeptide naturally present in a living organism is not "isolated," but the same polynucleotide or polypeptide separated from the coexisting materials
10 of its natural state is "isolated", as the term is employed herein. Moreover, a polynucleotide or polypeptide that is introduced into an organism by transformation, genetic manipulation or by any other recombinant method is "isolated" even if it is still present in said organism, which organism may be living or non-living.

"Secreted protein activity or secreted polypeptide activity" or "biological activity of
15 the secreted protein or secreted polypeptide" refers to the metabolic or physiologic function of said secreted protein including similar activities or improved activities or these activities with decreased undesirable side-effects. Also included are antigenic and immunogenic activities of said secreted protein.

"Secreted protein gene" refers to a polynucleotide comprising any of the attached
20 nucleotide sequences or allelic variants thereof and/or their complements.

"Polynucleotide" generally refers to any polyribonucleotide (RNA) or polydeoxribonucleotide (DNA), which may be unmodified or modified RNA or DNA.

"Polynucleotides" include, without limitation, single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA
25 that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, "polynucleotide" refers to triple-stranded regions comprising RNA or DNA or both RNA and DNA. The term "polynucleotide" also includes DNAs or RNAs containing one or more modified bases and DNAs or RNAs with backbones
30 modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications may be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically or metabolically modified forms of polynucleotides as typically found in nature, as well as the chemical forms of DNA and RNA characteristic of viruses and cells. "Polynucleotide" also embraces
35 relatively short polynucleotides, often referred to as oligonucleotides.

"Polypeptide" refers to any polypeptide comprising two or more amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres.

"Polypeptide" refers to both short chains, commonly referred to as peptides, oligopeptides or oligomers, and to longer chains, generally referred to as proteins. Polypeptides may contain amino acids other than the 20 gene-encoded amino acids. "Polypeptides" include amino acid sequences modified either by natural processes, such as post-translational processing, or by chemical modification techniques that are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications may occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present to the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched and branched cyclic polypeptides may result from post-translation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, biotinylation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cystine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination (see, for instance, *Proteins - Structure and Molecular Properties*, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York, 1993; Wold, F., *Post-translational Protein Modifications: Perspectives and Prospects*, 1-12, in *Post-translational Covalent Modification of Proteins*, B. C. Johnson, Ed., Academic Press, New York, 1983; Seifter *et al.*, "Analysis for protein modifications and nonprotein cofactors", *Meth Enzymol*, 182, 626-646, 1990, and Rattan *et al.*, "Protein Synthesis: Post-translational Modifications and Aging", *Ann NY Acad Sci*, 663, 48-62, 1992).

"Fragment" of a polypeptide sequence refers to a polypeptide sequence that is shorter than the reference sequence but that retains essentially the same biological function or activity as the reference polypeptide. "Fragment" of a polynucleotide sequence refers to a

polynucleotide sequence that is shorter than the reference sequence set forth in the Sequence Listing.

"Variant" refers to a polynucleotide or polypeptide that differs from a reference polynucleotide or polypeptide, but retains the essential properties thereof. A typical variant of a polynucleotide differs in nucleotide sequence from the reference polynucleotide. Changes in the nucleotide sequence of the variant may or may not alter the amino acid sequence of a polypeptide encoded by the reference polynucleotide. Nucleotide changes may result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptide encoded by the reference sequence, as discussed below. A typical variant of a polypeptide differs in amino acid sequence from the reference polypeptide. Generally, alterations are limited so that the sequences of the reference polypeptide and the variant are closely similar overall and, in many regions, identical. A variant and reference polypeptide may differ in amino acid sequence by one or more substitutions, insertions, deletions in any combination. A substituted or inserted amino acid residue may or may not be one encoded by the genetic code. Typical conservative substitutions include Gly, Ala; Val, Ile, Leu; Asp, Glu; Asn, Gln; Ser, Thr; Lys, Arg; and Phe and Tyr. A variant of a polynucleotide or polypeptide may be naturally occurring such as an allele, or it may be a variant that is not known to occur naturally. Non-naturally occurring variants of polynucleotides and polypeptides may be made by mutagenesis techniques or by direct synthesis. Also included as variants are polypeptides having one or more post-translational modifications, for instance glycosylation, phosphorylation, methylation, ADP ribosylation and the like. Embodiments include methylation of the N-terminal amino acid, phosphorylations of serines and threonines and modification of C-terminal glycines.

"Allele" refers to one of two or more alternative forms of a gene occurring at a given locus in the genome.

"Polymorphism" refers to a variation in nucleotide sequence (and encoded polypeptide sequence, if relevant) at a given position in the genome within a population.

"Single Nucleotide Polymorphism" (SNP) refers to the occurrence of nucleotide variability at a single nucleotide position in the genome, within a population. An SNP may occur within a gene or within intergenic regions of the genome. SNPs can be assayed using Allele Specific Amplification (ASA). For the process at least 3 primers are required. A common primer is used in reverse complement to the polymorphism being assayed. This common primer can be between 50 and 1500 bps from the polymorphic base. The other two (or more) primers are identical to each other except that the final 3' base wobbles to match one of the two (or more) alleles that make up the polymorphism. Two (or more) PCR

reactions are then conducted on sample DNA, each using the common primer and one of the Allele Specific Primers.

"Splice Variant" as used herein refers to cDNA molecules produced from RNA molecules initially transcribed from the same genomic DNA sequence but which have undergone alternative RNA splicing. Alternative RNA splicing occurs when a primary RNA transcript undergoes splicing, generally for the removal of introns, which results in the production of more than one mRNA molecule each of that may encode different amino acid sequences. The term splice variant also refers to the proteins encoded by the above cDNA molecules.

"Identity" reflects a relationship between two or more polypeptide sequences or two or more polynucleotide sequences, determined by comparing the sequences. In general, identity refers to an exact nucleotide to nucleotide or amino acid to amino acid correspondence of the two polynucleotide or two polypeptide sequences, respectively, over the length of the sequences being compared.

"% Identity" - For sequences where there is not an exact correspondence, a "% identity" may be determined. In general, the two sequences to be compared are aligned to give a maximum correlation between the sequences. This may include inserting "gaps" in either one or both sequences, to enhance the degree of alignment. A % identity may be determined over the whole length of each of the sequences being compared (so-called global alignment), that is particularly suitable for sequences of the same or very similar length, or over shorter, defined lengths (so-called local alignment), that is more suitable for sequences of unequal length.

"Similarity" is a further, more sophisticated measure of the relationship between two polypeptide sequences. In general, "similarity" means a comparison between the amino acids of two polypeptide chains, on a residue by residue basis, taking into account not only exact correspondences between a between pairs of residues, one from each of the sequences being compared (as for identity) but also, where there is not an exact correspondence, whether, on an evolutionary basis, one residue is a likely substitute for the other. This likelihood has an associated "score" from which the "% similarity" of the two sequences can then be determined.

Methods for comparing the identity and similarity of two or more sequences are well known in the art. Thus for instance, programs available in the Wisconsin Sequence Analysis Package, version 9.1 (Devereux J et al, Nucleic Acids Res, 12, 387-395, 1984, available from Genetics Computer Group, Madison, Wisconsin, USA), for example the programs BESTFIT and GAP, may be used to determine the % identity between two polynucleotides and the %

identity and the % similarity between two polypeptide sequences. BESTFIT uses the "local homology" algorithm of Smith and Waterman (J Mol Biol, 147,195-197, 1981, Advances in Applied Mathematics, 2, 482-489, 1981) and finds the best single region of similarity between two sequences. BESTFIT is more suited to comparing two polynucleotide or two polypeptide sequences that are dissimilar in length, the program assuming that the shorter sequence represents a portion of the longer. In comparison, GAP aligns two sequences, finding a "maximum similarity", according to the algorithm of Neddleman and Wunsch (J Mol Biol, 48, 443-453, 1970). GAP is more suited to comparing sequences that are approximately the same length and an alignment is expected over the entire length. Preferably, the parameters "Gap Weight" and "Length Weight" used in each program are 50 and 3, for polynucleotide sequences and 12 and 4 for polypeptide sequences, respectively. Preferably, % identities and similarities are determined when the two sequences being compared are optimally aligned.

Other programs for determining identity and/or similarity between sequences are also known in the art, for instance the BLAST family of programs (Altschul S F et al, J Mol Biol, 215, 403-410, 1990, Altschul S F et al, Nucleic Acids Res., 25:389-3402, 1997, available from the National Center for Biotechnology Information (NCBI), Bethesda, Maryland, USA and accessible through the home page of the NCBI at www.ncbi.nlm.nih.gov) and FASTA (Pearson W R, Methods in Enzymology, 183, 63-99, 1990; Pearson W R and Lipman D J, Proc Nat Acad Sci USA, 85, 2444-2448, 1988, available as part of the Wisconsin Sequence Analysis Package).

Preferably, the BLOSUM62 amino acid substitution matrix (Henikoff S and Henikoff J G, Proc. Nat. Acad Sci. USA, 89, 10915-10919, 1992) is used in polypeptide sequence comparisons including where nucleotide sequences are first translated into amino acid sequences before comparison.

Preferably, the program BESTFIT is used to determine the % identity of a query polynucleotide or a polypeptide sequence with respect to a reference polynucleotide or a polypeptide sequence, the query and the reference sequence being optimally aligned and the parameters of the program set at the default value, as hereinbefore described.

"Identity Index" is a measure of sequence relatedness which may be used to compare a candidate sequence (polynucleotide or polypeptide) and a reference sequence. Thus, for instance, a candidate polynucleotide sequence having, for example, an Identity Index of 0.95 compared to a reference polynucleotide sequence is identical to the reference sequence except that the candidate polynucleotide sequence may include on average up to five differences per each 100 nucleotides of the reference sequence. Such differences are selected from the group

consisting of at least one nucleotide deletion, substitution, including transition and transversion, or insertion. These differences may occur at the 5' or 3' terminal positions of the reference polynucleotide sequence or anywhere between these terminal positions, interspersed either individually among the nucleotides in the reference sequence or in one or more

5 contiguous groups within the reference sequence. In other words, to obtain a polynucleotide sequence having an Identity Index of 0.95 compared to a reference polynucleotide sequence, an average of up to 5 in every 100 of the nucleotides of the in the reference sequence may be deleted, substituted or inserted, or any combination thereof, as hereinbefore described. The same applies *mutatis mutandis* for other values of the Identity Index, for instance 0.96, 0.97,

10 0.98 and 0.99.

Similarly, for a polypeptide, a candidate polypeptide sequence having, for example, an Identity Index of 0.95 compared to a reference polypeptide sequence is identical to the reference sequence except that the polypeptide sequence may include an average of up to five differences per each 100 amino acids of the reference sequence. Such differences are selected

15 from the group consisting of at least one amino acid deletion, substitution, including conservative and non-conservative substitution, or insertion. These differences may occur at the amino- or carboxy-terminal positions of the reference polypeptide sequence or anywhere between these terminal positions, interspersed either individually among the amino acids in the reference sequence or in one or more contiguous groups within the reference sequence. In

20 other words, to obtain a polypeptide sequence having an Identity Index of 0.95 compared to a reference polypeptide sequence, an average of up to 5 in every 100 of the amino acids in the reference sequence may be deleted, substituted or inserted, or any combination thereof, as hereinbefore described. The same applies *mutatis mutandis* for other values of the Identity Index, for instance 0.96, 0.97, 0.98 and 0.99.

25 The relationship between the number of nucleotide or amino acid differences and the Identity Index may be expressed in the following equation:

$$n_a \leq x_a - (x_a \cdot I),$$

in which:

n_a is the number of nucleotide or amino acid differences,

30 x_a is the total number of nucleotides or amino acids in a sequence set forth in the Sequence Listing,

I is the Identity Index,

\cdot is the symbol for the multiplication operator, and

in which any non-integer product of x_a and l is rounded down to the nearest integer prior to subtracting it from x_a .

"Homolog" is a generic term used in the art to indicate a polynucleotide or polypeptide sequence possessing a high degree of sequence relatedness to a reference sequence. Such relatedness may be quantified by determining the degree of identity and/or similarity between the two sequences as hereinbefore defined. Falling within this generic term are the terms "ortholog", and "paralog". "Ortholog" refers to a polynucleotide or polypeptide that is the functional equivalent of the polynucleotide or polypeptide in another species. "Paralog" refers to a polynucleotide or polypeptide that within the same species which is functionally similar.

"Fusion protein" refers to a protein encoded by two, often unrelated, fused genes or fragments thereof. In one example, EP-A-0 464 533-A discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, employing an immunoglobulin Fc region as a part of a fusion protein is advantageous for use in therapy and diagnosis resulting in, for example, improved pharmacokinetic properties [see, e.g., EP-A 0232 262]. On the other hand, for some uses it would be desirable to be able to delete the Fc part after the fusion protein has been expressed, detected and purified.

All publications and references, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference in their entirety as if each individual publication or reference were specifically and individually indicated to be incorporated by reference herein as being fully set forth. Any patent application to which this application claims priority is also incorporated by reference herein in its entirety in the manner described above for publications and references.

Table I.

Gene Name	GSK Gene ID	Nucleic Acid SEQ ID NO's	Corresponding Protein SEQ ID NO's
sbg101452SLITa	101452	SEQ ID NO:1	SEQ ID NO:27
sbg29046CYSa	29046a	SEQ ID NO:2	SEQ ID NO:28
sbg29046CYSb	29046b	SEQ ID NO:3 SEQ ID NO:4	SEQ ID NO:29 SEQ ID NO:30
sbg37149SLITb	37149	SEQ ID NO:5	SEQ ID NO:31
sbg36267SLIta	36267	SEQ ID NO:6	SEQ ID NO:32
sbg35579MELAA	35579	SEQ ID NO:7 SEQ ID NO:8	SEQ ID NO:33 SEQ ID NO:34
SBh69447. Triglyceride Lipase	69447	SEQ ID NO:9	SEQ ID NO:35
SBh86614.TrypI	86614	SEQ ID NO:10 SEQ ID NO:11	SEQ ID NO:36 SEQ ID NO:37
sbg106886DELTAa	106886	SEQ ID NO:12	SEQ ID NO:38
sbg35779THYa	35779	SEQ ID NO:13	SEQ ID NO:39
sbg15130INHb	15130	SEQ ID NO:14 SEQ ID NO:15	SEQ ID NO:40 SEQ ID NO:41
SBh26548.homebox	26548	SEQ ID NO:16	SEQ ID NO:42
sbg26991CERUa	26991	SEQ ID NO:17	SEQ ID NO:43
sbg35851PEROa	35851	SEQ ID NO:18 SEQ ID NO:19	SEQ ID NO:44 SEQ ID NO:45
sbg36274SLITa	36274	SEQ ID NO:20	SEQ ID NO:46
sbg34575SLITa	34575	SEQ ID NO:21	SEQ ID NO:47
SBh71706.NIAP	71706	SEQ ID NO:22 SEQ ID NO:23	SEQ ID NO:48 SEQ ID NO:49
SBh77492.Breast Specific BS200	77492	SEQ ID NO:24 SEQ ID NO:25	SEQ ID NO:50 SEQ ID NO:51
sbg115305LRRa	115305	SEQ ID NO:26	SEQ ID NO:52

Table II

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg101452SLITa	Slit-like membrane glycoprotein	GB:AL138498 Submitted (07-DEC-2000) by Genoscope - Centre National de Sequencage : BP 191 91006 EVRY cedex - FRANCE	KIAA1246 protein,gi:6330833 Submitted (04-OCT-1999) by Osamu Ohara, Kazusa DNA Research Institute, Laboratory of DNA Technology; 1532-3 Yana, Kisarazu, Chiba 292-0812, Japan	Membrane-bound
sbg29046CYSa	Cystatin	GB:AL121894 Submitted on Feb 18,2000 by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK	Human cystatin family member gi :9944240 Submitted (25-OCT-2000) Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Secreted
sbg29046CYSb	Cystatin	GB:AL121894 Submitted on Feb 18,2000 by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK	Novel human cystatin-related protein geneseqp:Y53771 (KARO-) KAROLINSKA INNOVATIONS AB WO9958565-A1, 18-NOV-99	Secreted
sbg37149SLITb	Slit-like membrane glycoprotein	GB:Z94160 Submitted on Dec8, 1999, Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human putative leucine rich protein gi:3191975 Submitted (08-DEC-1999) Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Membrane-bound
sbg36267SLITa	Slit 3-like membrane glycoprotein	GB:AL080239 Submitted on Jan10, 2000, by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human KIAA0918 protein, gi :4240325 Nagase,T., Ishikawa,K., Suyama,M., Kikuno,R., Hirosawa,M., Miyajima,N., Tanaka,A., Kotani,H., Nomura,N. and Ohara,O. DNA Res. 5 (6), 355-364 (1998)	Membrane-bound
sbg35579MELAa	Brain-specific transmembrane glycoprotein	GB:AC018477 Submitted (12-DEC-1999) by Human Genome Sequencing Center, Department of Molecular and Human Genetics, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, USA	Human KIAA1484 protein, gi: 7959229 Nagase,T., Kikuno,R., Ishikawa,K., Hirosawa,M. and Ohara,O. DNA Res. 7 (2), 143-150 (2000).	Membrane-bound
SBh69447. Triglyceride Lipase	Triglyceride lipase	GB:AC011277 Submitted (05-OCT-1999) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Human gastric lipase, gi:4758676 Bodmer,M.W., Angal,S., Yarranton,G.T., Harris,T.J., Lyons,A., King,D.J., Pieroni,G., Riviere,C., Verger,R. and Lowe,P.A. Biochim. Biophys. Acta 909 (3), 237-244 (1987)	Secreted

Table II Cont

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
SBh86614.Tryp1	Serine protease	JGI:RPCI-11± 388M20 Found at Joint Genome Institute	Human PRO351 protein, gene: Y41704 GENENTECH INC WO9946281-A2, 16-SEP-99	Secreted
sbg106886DELTAa	DELTAa	GB:AC021391 Submitted on JAN 16, 2000, Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Rat preadipocyte factor, gi: 802014 Carlsson,C., Tornehave,D., Lindberg,K., Galante,P., Billestrup,N., Michelsen,B., Larsson,L.I. and Nielsen,J.H. Endocrinology 138 (9), 3940-3948 (1997)	Secreted
sbg35779THYa	Thyroxine binding globulin	GB:AL132990 Submitted (27-JAN-2000) by Genoscope - Centre National de Sequencage :BP 191 91006 EVRY cedex	Human PRO1337 GENENTECH INC WO200012708-A2, 09-MAR-00	Secreted
sbg15130INHaa	Leukocyte protease inhibitor	SC:Z93016 Submitted (31-JUL-2000) Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human serine protease inhibitor, gene: Y28645 Human Genome Sci Inc WO199940183-A1, 12-AUG-99	Secreted
SBh26548.homebox	LBX, HOX, DLX	GB:AC005041 Sulston,J.E. and Waterston,R. Genome Res. 8 (11), 1097-1108 (1998)	Mouse lady bird-like homeobox 2 homolog, gi: 6754512 Chen,F., Liu,K.C. and Epstein,J.A. Mech. Dev. (1999).	Nucleus
sbg26991CERUa	Ceruloplasmin precursor	GB:AC010909 Submitted (26-SEP-1999) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Human ceruloplasmin, gi: 1070458 Takahashi,N., Ortel,T.L. and Putnam,F.W. Proc. Natl. Acad. Sci. U.S.A. 81 (2), 390-394 (1984).	Secreted
sbg35851PEROa	Slit-like membrane glycoprotein	GB:AF038458 Submitted (12-DEC-1997) Human Genome Center, Lawrence Livermore National Laboratory, 7000 East Ave., Livermore, CA 94551, USA	Human KIAA1246 protein, gi: 6330833 Submitted (04-OCT-1999) by Osamu Ohara, Kazusa DNA Research Institute, Laboratory of DNA Technology; 1532-3 Yana, Kisarazu, Chiba 292-0812, Japan	Membrane-bound
sbg36274SLITa	Slit-like membrane glycoprotein	GB:AL109653 Submitted (22-NOV-1999) Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human novel protein, gi: 11877257 Submitted (20-JAN-2000) Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA	Membrane-bound

Table II Cont

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg34575SLITa	Slit-like membrane glycoprotein	GB:AC005343 Submitted (31-JUL-1998) by Molecular and Human Genetics, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, USA.	pineal gland specific gene-1 protein, geneseq: W09405 Huaman Genome Sci Inc WO9639158-A1, 12-DEC-96	Membrane-bound
SBh71706.NIAP	Apoptosis inhibitory protein	GB:AL121653 Submission (29-FEB-2000) by Genoscope.	Human hypothetical protein, weakly similar to mouse neuronal apoptosis inhibitory protein 2, gi:9367840 Submitted (15-JUL-2000) by Dept. Genetica Molecular, Institut de Recerca Oncologica (IRO), Hospital Duran i Reynals, Av. Gran Via s/n Km 2,7 L'Hospitalet de Llobregat, 08907 Barcelona, Catalunya, SPAIN.	Cytosolic
SBh77492.Breast Specific BS200	EGF-related protein	SC:Z82214,GB:Z99756 Submitted (08-DEC-1999) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Mouse EGF-related protein SCUBE1, gi: 10998440 Submitted (08-JUN-2000) Mammalian Genetics Unit, MRC Harwell, Chilton, Didcot, Oxon OX11 0RD, United Kingdom.	Secreted
sbgl15305LRRa	Lucine-rich repeat (LRR)	GB:AC023484 Submitted (14-FEB-2000) Human Genomic Center, Institute of Genetics, Chinese Academy of Sciences, Datun Road, Beijing, Beijing 100101, P.R.China	Muse leucine rich repeat protein 1, gi:678724 Taguchi A, Wanaka A, Mori T, Matsumoto K, Imai Y, Tagaki T, Tohyama M, 1996, Brain Res Mol Brain Res;35:31-4.	Membrane-bound

Table III.

Gene Name	Uses	Associated Diseases
sbgl01452SLITa	An embodiment of the invention is the use of sbgl01452SLITa, a member of the slit protein family, for diagnosis and treatment of nervous and muscular diseases. This is because other members of the slit protein family may be necessary for CNS development. In addition, sbgl01452SLITa shows homology to leucine-rich repeat proteins, which demonstrates significant functions in neural development. It is thus possible that similar molecules play a crucial role in the morphogenesis of the mammalian nervous system (Taniguchi H, Tohyama M, Takagi T. Brain Res Mol Brain Res 1996 Feb;36(1):45-52).	Gastrointestinal ulceration, Zollinger-Ellison syndrome, congenital microvillus atrophy, skin diseases
sbg29046CYSa	An embodiment of the invention is the use of sbg29046CYSa to inhibit tumor formation and metastasis and may also be involved in natural tissue remodeling events such as bone resorption and embryo implantation. Close Homologs of sbg29046CYSa are cysteine protease inhibitors known as cystatins. Cystatins and their target proteases have been associated with tumor formation and metastasis, but also are involved in natural tissue remodeling events such as bone resorption and embryo implantation (Tohonen V., Osterlund C., and Nordqvist K., 1998 Proc Natl Acad Sci U S A 95(24):14208-13). Cystatin is a natural and specific inhibitor of the cysteine proteases generating in cancer invasion. The level of cystatin determination in serum and tissue extracts can be the clinical diagnostic and prognostic parameters in human cancers (Kos J., Stabuc B., Cimerman N., and Brunner N., 1998. Clin Chem 44(12):2556-7).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing, inflammation metastasis, amyloid angiopathies, and progressive myoclonus epilepsy
sbg29046CYSb	An embodiment of the invention is the use of sbg29046CYSb to inhibit tumor formation and metastasis and may also be involved in natural tissue remodeling events such as bone resorption and embryo implantation. Close homologs of sbg29046CYSa are cysteine protease inhibitors known as cystatins. Cystatins and their target proteases have been associated with tumor formation and metastasis, but also are involved in natural tissue remodeling events such as bone resorption and embryo implantation (Tohonen V., Osterlund C., and Nordqvist K., 1998 Proc Natl Acad Sci U S A 95(24):14208-13). Cystatin is a natural and specific inhibitor of the cysteine proteases generating in cancer invasion. The level of cystatin determination in serum and tissue extracts can be the clinical diagnostic and prognostic parameters in human cancers (Kos J., Stabuc B., Cimerman N., and Brunner N., 1998. Clin Chem 44(12):2556-7).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing, inflammation metastasis, amyloid angiopathies, and progressive myoclonus epilepsy
sbg37149SLITb	An embodiment of the invention is the use of sbg37149SLITb, a member of human slit-like proteins, which may be necessary for CNS development, and therefore can be useful for diagnosis and treatment of nervous and muscular diseases. In addition, sbg37149SLITb shows similarity to leucine-rich repeat proteins, and may also demonstrate significant functions in neural development. It has been shown that expression of slit genes is associated with neuronal migration in the developing forebrain (Hu H, Neuron 703-11,1999). It is thus possible that sbg37149SLITb plays a crucial role in the morphogenesis of the mammalian nervous system (Taniguchi H, Tohyama M, Takagi T. Brain Res Mol Brain Res 1996 Feb;36(1):45-52)	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing, inflammation, and diseases in spinal cord, thyroid gland, ovary, prostate, renal gland, small intestine, heart, trachea, thymus, lymph node, and muscular system

Table III Cont

Gene Name	Uses	Associated Diseases
sbg36267SLITa	An embodiment of the invention is the use of sbg36267SLITa to treat gastrointestinal ulceration as well as prevention and treatment of diseases in spinal cord, thyroid gland, ovary, prostate, renal gland, small intestine, heart, trachea, thymus, lymph node, muscular system and colon. sbg36267SLITa is exploitable in similar ways to a close homolog human KIAA0918 protein, which is functionally related to cell signaling/communication, cell structure/motility and nucleic acid management. A close homolog of sbg36267SLITa is PRO266 and human slit 3 mature protein.	Gastrointestinal ulceration, diseases in spinal cord, thyroid gland, ovary, prostate, renal gland, small intestine, heart, trachea, thymus, lymph node, muscular system and colon
sbg35579MELAA	An embodiment of the invention is the use of sbg35579MELAA The closest homologue to this novel protein is human KIAA1484 protein which is derived from brain-specific cDNA library and functionally related to cell signaling/communication, cell structure/motility and nucleic acid management. Other close homologs to sbg35579MELAA are human KIAA1246, also derived from brain-specific cDNA library and human brain-specific transmembrane glycoprotein B09968. B09968 has a typical PDZ protein binding motif and functions as a cellular signal transducer, useful in developing drugs for treating nervous diseases	Gastrointestinal ulceration, diseases in spinal cord, thyroid gland, ovary, prostate, renal gland, small intestine, heart, trachea, thymus, lymph node, muscular system and colon.
SBh69447. Triglyceride Lipase	An embodiment of the invention is the use of SBh69447. Triglyceride Lipase, a member of gastric lipases, for oral administration to treat lipase deficiency in cystic fibrosis and pancreatitis. Some gastric lipases are also useful therapeutically for absorption of ingested fat in patients with mucoviscidiosis of fat and defective transesterification (WO8601532-A).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing, inflammation, gastric lipase deficiency, cystic fibrosis, Pancreatitis, altered absorption of fat, gastrointestinal disorders, defective biocatalysis, mucoviscidosis, poor enzymatic bioconversion of fat, cystic fibrosis, pancreatitis diseases
SBh86614.Tryp1	An embodiment of the invention is the use of SBh86614.Tryp1, a member of the mast cell protease/ trypase family, for treatment of undesirable clot formation such as myocardial infarction, during angioplasty and all surgical procedures that require decreased blood clot formation and may also be involved in tumor growth and fertility. Other homologs of the mast cell protease/ trypase family have been identified in WO9836054-A1 and WO9824886-A1.	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorder, inflammation, blood coagulation disorders, cancers and cellular adhesion disorders, deep vein thrombosis, myocardial infarction
sbg106886 DELTAa	An embodiment of the invention is the use of sbg106886DELTAa in cellular interactions and fetal development. Close homologs of sbg106886DELTAa are involved in cell-to-cell communications in mammalian embryos through the Notch signaling pathway, and therefore may have a role in cellular interactions (Artavanis-Tsakonas et al., 1995, Science 268: 225-232). It has been shown that mouse Delta1 protein is essential for normal somitogenesis and neuronal differentiation, and Delta1 expression can be detected during organogenesis and fetal development (Beckers J., Clark A., Wunsch K., Hrabe De Angelis M., Gossler A. 1999, Mech Dev 84:165-8).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing, inflammation

Table III Cont.

Gene Name	Uses	Associated Diseases
sbg35779THY _a	An embodiment of the invention is the use of sbg35779THY _a , a secreted protein, in the diagnosis and also in the treatment of thyroid and liver diseases, treatment of septic shock, pancreatitis, coagulation disorders, and microbial diseases. Close homologs of sbg35779THY _a are Mutant Human alpha-1-antichymotrypsin with Arg(358) and Alpha-1-antichymotrypsin (Leu358Arg).	Thyroid and liver diseases, septic shock, pancreatitis, coagulation disorders, microbial diseases
sbgl5130INH _a	An embodiment of the invention is the use of sbgl5130INH _a , a secreted protein, in developing products for treating e.g. immune disorders, cancers, inflammation, transplant rejection or infections. A close homolog of sbgl5130INH _a is mouse and rat secretory leukocyte protease inhibitors (SLPI). Transfection of macrophages with SLPI have been shown to suppress LPS-induced activation of NF-kappa B and production of nitric oxide and TNF alpha (Jin, F.Y., Nathan, C., Radzioch, D. and Ding, A. Cell 88 (3), 417-426 (1997)).	Immune disorders, cancers, inflammation, transplant rejection or infections, disorders in fetal development
SBh26548.homebox	An embodiment of the invention is the use of SBh26548 homebox to enhance bone thickness and increase bone density at the site of application or may affect developmental conditions if expressed in the thymus or T cells. Close homologs of SBh26548 homebox are members of HOX and DLX (US5850002-A and WO9943784-A2).	Autoimmune disorder, hematopoietic disorder, wound healing disorder, cancer, inflammation, viral and bacterial infection, autosomal dominant disorder, bone defects, osteoporosis, trauma, periodontal defects
sbg26991CERU _a	An embodiment of the invention is the use of sbg26991CERU _a to reduce the loss of essential ferroxidases. Copper is an essential trace metal which plays a fundamental role in the biochemistry of the human nervous system. Close homologs of sbg26991CERU _a are Ceruloplasmins. Ceruloplasmins are plasma metalloproteins that contains 95% of the copper found in human plasma and inherited loss of this essential ferroxidase is associated with progressive neurodegeneration of the retina and basal ganglia (Waggoner DJ, Bartnikas TB, Gitlin JD, 1999 Neurobiol Dis 6(4):221-30). Ceruloplasmin deficiency leads to iron accumulation and causes damage to a variety of tissues and organs. Serum ceruloplasmin determination can be part of diagnostic procedures of Wilson's disease, an inherited copper storage disease.	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorder, inflammation, and progressive neurodegeneration of the retina and basal ganglia
sbg35851PERO _a	An embodiment of the invention is the use of sbg35851PERO _a , a member of the slit protein family, for diagnosis and treatment of nervous and muscular diseases. In addition, sbg35851PERO _a shows homology to leucine-rich repeat proteins, which demonstrates significant functions in neural development. It is thus possible that similar molecules play a crucial role in the morphogenesis of the mammalian nervous system (Taniguchi H, Tohyama M, Takagi T. Brain Res Mol Brain Res 1996 Feb;36(1):45-52).	Cancer, Gastrointestinal ulceration, Zollinger-Ellison syndrome, congenital microvillus atrophy, skin diseases, diseases associated with nervous system.
sbg36274SLIT _a	An embodiment of the invention is the use of sbg36274SLIT _a , a member of human slit-like proteins, which may be necessary for CNS development, and therefore can be useful for diagnosis and treatment of nervous and muscular diseases. A close homolog of sbg36274SLIT _a is insulin-like growth factor. Insulin-like growth factors may be used to treat patients with growth hormone receptor deficiency (GHRD) (Fielder PJ, Gargosky SE, Vaccarello M, Wilson K, Cohen P, Diamond F, Guevara-Aguirre J, Rosenbloom AL, and Rosenfeld RG 1993. Acta Paediatr Suppl 388:40-3).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorder, inflammation, gastrointestinal ulceration, and diseases in spinal cord, thyroid gland, ovary, prostate, renal gland, small intestine, heart, trachea, thymus, lymph node, and muscular system

TABLE III Cont

Gene Name	Uses	Associated Diseases
sbg34575SLITa	An embodiment of the invention is the use of sbg34575SLITa, a member of human slit-like proteins, which may be necessary for CNS development, and therefore can be useful for diagnosis and treatment of nervous and muscular diseases. A close homolog of sbg34575SLITa is leucine-rich repeat proteins(BAA85972, mouse ISLR), which also demonstrates significant functions in neural development (Nagasawa, A., Kudoh, J., Noda, S., Mashima, Y., Wright, A., Oguchi, Y., and Shimizu, N. Genomics 61 (1), 37-43, 1999). It has been shown that expression of slit genes is associated with neuronal migration in the developing forebrain (Hu H, Neuron 23:703-11, 1999). It is thus possible that similar molecules play a crucial role in the morphogenesis of the mammalian nervous system (Taniguchi H, Tohyama M, Takagi T. Brain Res Mol Brain Res 1996 36(1):45-52).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorder, inflammation, gastrointestinal ulceration, and diseases in spinal cord, thyroid gland, ovary, prostate, small intestine, heart, trachea, thymus, lymph node, muscular system and colon
SBh71706.NIAP	An embodiment of the invention is the use of SBh71706.NIAP in the suppression of apoptosis. Related polypeptides have been used for treating regulation of cellular proliferation and differentiation and cell survival. The NIAP prevent motor neuron apoptosis induced by a variety of signals. These proteins do contain 3 BIR(Baculoviral Inhibition of apoptosis protein repeats (LISTON, P. Nature 379 (6563), 349-353 (1996).	Autoimmune disorder, hematopoietic disorder, wound healing disorder, viral and bacterial infection, cancer, AIDS, amyotrophic lateral sclerosis, infertility, human spinal muscular atrophy and neurodegenerative disorder
SBh77492.Breast Specific BS200	An embodiment of the invention is the use of SBh77492.Breast Specific BS200 in regulating vascular smooth muscle cell proliferation. A close homolog of SBh77492.Breast Specific BS200 is EEGF protein. EEGF protein is useful for enhancing neurological functions or treating neoplasia and other disorders (LI HS and OLSEN H, New isolated extracellular/epidermal growth factor, Patent Accession Number W79739, HUMAN GENOME SCI INC).	Cancer, autoimmune disorders, wound healing disorders, infections, and hematopoietic disorders
sbgl15305LRRa	An embodiment of the invention is the use of sbgl15305LRRa, a Leucine-rich repeat (LRR) protein, in neuronal development and the adult nervous systems as cell adhesion molecules. Close homologs of sbgl15305LRRa are connectin, slit, chaoptin, and toll. These LRR proteins possibly have important roles in neuronal development and the adult nervous systems as cell adhesion molecules (Taguchi A, Wanaka A, Mori T, Matsumoto K, Imai Y, Tagaki T, Tohyama M, 1996, Brain Res Mol Brain Res 35:31-4). Leucine-rich repeat protein family has been implicated in protein-protein interactions, such as cell adhesion or receptor-ligand binding. At least one LRR was shown to be specifically expressed on B cells, suggesting its role in immunization (Miyake K, Yamashita Y, Ogata M, Sudo T, Kimoto M, 1995. J Immunol 154:3333-40). Some studies have shown that brain injury can cause over expression of neuronal LRR, suggesting that neuronal LRR may be an important component of the pathophysiological response to brain injury (Ishii N, Wanaka A, Tohyama M, Brain Res Mol Brain Res 1996 Aug;40(1):148-52).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorder, inflammation, gastrointestinal ulceration, diseases in spinal cord, thyroid gland, heart, trachea, thymus, lymph node, muscular system, and nervous system

Table IV. Quantitative, Tissue-specific mRNA expression detected using SybrMan

Quantitative, tissue-specific, mRNA expression patterns of the genes were measured using SYBR-Green Quantitative PCR (Applied Biosystems, Foster City, CA; see Schmittgen T.D. et al., Analytical Biochemistry 285:194-204, 2000) and human cDNAs prepared from various human tissues. Gene-specific PCR primers were designed using the first nucleic acid sequence listed in the Sequence List for each gene. Results are presented as the number of copies of each specific gene's mRNA detected in 1ng mRNA pool from each tissue. Two replicate mRNA measurements were made from each tissue RNA.

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. \pm range for 2 data points per tissue)									
	Brain	Heart	Lung	Liver	Kidney	Skeletal muscle	Intestine	Spleen/lymph	Placenta	Testis
sbgl0145 2SLITa	3389 \pm 33	174 \pm 11	187 \pm 29	-6 \pm 2	112 \pm 4	64 \pm 5	159 \pm 7	147 \pm 8	209 \pm 37	563 \pm 37
sbg29046 CYSa	338 \pm 60	385 \pm 69	735 \pm 29	138 \pm 41	592 \pm 36	218 \pm 25	186 \pm 35	348 \pm 52	839 \pm 65	46124 \pm 22605
sbg29046 CYSb	951 \pm 69	1121 \pm 74	358 \pm 110	364 \pm 44	871 \pm 128	1133 \pm 203	347 \pm 101	612 \pm 18	601 \pm 12	591 \pm 51
sbg37149 SLITb	4989 \pm 18	51 \pm 10	457 \pm 41	148 \pm 12	769 \pm 90	17 \pm 2	31 \pm 11	37 \pm 14	10 \pm 6	346 \pm 10
sbg36267 SLITa	2976 \pm 186	258 \pm 8	127 \pm 30	2 \pm 0	1374 \pm 13	2188 \pm 72	44 \pm 1	81 \pm 5	113 \pm 4	242 \pm 1
sbg35579 MELAA	4630 \pm 1163	5518 \pm 506	6114 \pm 1422	1701 \pm 140	5876 \pm 1366	4017 \pm 291	1918 \pm 25	4310 \pm 279	5247 \pm 1	3589 \pm 148
SBh69447 .Triglyceride Lipase	1 \pm 0	5 \pm 1	6 \pm 6	-7 \pm 6	3 \pm 0	1 \pm 0	-2 \pm 3	4 \pm 1	200 \pm 8	18 \pm 7
SBh86614 .TrypI	742 \pm 82	392 \pm 18	487 \pm 24	642 \pm 6	576 \pm 12	369 \pm 53	234 \pm 15	547 \pm 25	662 \pm 2	550 \pm 4
sbgl0688 DELTAa	1308 \pm 49	520 \pm 19	340 \pm 66	127 \pm 11	418 \pm 24	264 \pm 39	130 \pm 21	269 \pm 21	538 \pm 99	558 \pm 116
sbg35779 THYa	2 \pm 1	2 \pm 1	21 \pm 1	-4 \pm 8	2 \pm 1	-5 \pm 8	26 \pm 2	886 \pm 38	7 \pm 2	6 \pm 5
sbgl51301 NHa	4 \pm 1	6 \pm 2	209 \pm 2	-4 \pm 6	42 \pm 1	-2 \pm 8	9 \pm 5	14 \pm 0	12 \pm 4	133 \pm 9
SBh26548 .home-box	56 \pm 3	85 \pm 5	111 \pm 18	273 \pm 1	149 \pm 12	80 \pm 17	86 \pm 12	88 \pm 8	120 \pm 49	81 \pm 35
sbg26991 CERUa	1 \pm 0	4 \pm 2	2 \pm 2	1 \pm 3	4 \pm 0	-1 \pm 0	4 \pm 0	2 \pm 2	9 \pm 0	26 \pm 8
sbg35851 PEROa	83 \pm 20	31 \pm 1	37 \pm 17	29 \pm 5	53 \pm 14	35 \pm 8	17 \pm 4	25 \pm 13	36 \pm 9	38 \pm 3
sbg36274 SLITa	8770 \pm 345	598 \pm 8	591 \pm 57	7 \pm 5	518 \pm 82	75 \pm 9	253 \pm 13	2847 \pm 37	13 \pm 1	278 \pm 6
sbg34575 SLITa	2045 \pm 346	2 \pm 0	5 \pm 0	-14 \pm 2	-2 \pm 4	-4 \pm 3	0 \pm 0	26 \pm 7	10 \pm 0	45 \pm 6
SBh71706 .NIAP	251 \pm 9	535 \pm 25	1055 \pm 55	122 \pm 36	144 \pm 7	322 \pm 15	149 \pm 5	1081 \pm 67	740 \pm 27	387 \pm 17
SBh77492 .Breast Specific BS200	154 \pm 4	134 \pm 4	1954 \pm 135	325 \pm 57	981 \pm 13	60 \pm 6	700 \pm 15	1246 \pm 5	586 \pm 30	2614 \pm 69
sbgl1965 2TYRa	43 \pm 11	132 \pm 21	25 \pm 8	10 \pm 7	122 \pm 15	24 \pm 10	22 \pm 11	30 \pm 8	15 \pm 15	615 \pm 4
sbgl1530 5LRRa	7057 \pm 326	289 \pm 1	1122 \pm 88	111 \pm 4	547 \pm 5	6178 \pm 84	361 \pm 12	896 \pm 8	377 \pm 18	9121 \pm 120

Table V. Additional diseases based on mRNA expression in specific tissues

Tissue Expression	Additional Diseases
Brain	Neurological and psychiatric diseases, including Alzheimers, parasupranuclear palsey, Huntington's disease, myotonic dystrophy, anorexia, depression, schizophrenia, headache, amnesias, anxiety disorders, sleep disorders, multiple sclerosis
Heart	Cardiovascular diseases, including congestive heart failure, dilated cardiomyopathy, cardiac arrhythmias, Hodgson's Disease, myocardial infarction, cardiac arrhythmias
Lung	Respiratory diseases, including asthma, Chronic Obstructive Pulmonary Disease, cystic fibrosis, acute bronchitis, adult respiratory distress syndrome
Liver	Dyslipidemia, hypercholesterolemia, hypertriglyceridemia, cirrhosis, hepatic encephalopathy, fatty hepatocirrhosis, viral and nonviral hepatitis, Type II Diabetes Mellitis, impaired glucose tolerance
Kidney	Renal diseases, including acute and chronic renal failure, acute tubular necrosis, cystinuria, Fanconi's Syndrome, glomerulonephritis, renal cell carcinoma, renovascular hypertension
Skeletal muscle	Eulenburg's Disease, hypoglycemia, obesity, tendinitis, periodic paralyses, malignant hyperthermia, paramyotonia congenita, myotonia congenita
Intestine	Gastrointestinal diseases, including Myotonia congenita, Ileus, Intestinal Obstruction, Tropical Sprue, Pseudomembranous Enterocolitis
Spleen/lymph	Lymphangiectasia, hypersplenism, angiomas, ankylosing spondylitis, Hodgkin's Disease, macroglobulinemia, malignant lymphomas, rheumatoid arthritis
Placenta	Choriocarcinoma, hydatidiform mole, placenta previa
Testis	Testicular cancer, male reproductive diseases, including low testosterone and male infertility
Pancreas	Diabetic ketoacidosis, Type 1 & 2 diabetes, obesity, impaired glucose tolerance

What is claimed is:

1. An isolated polypeptide selected from the group consisting of:
 - (a) an isolated polypeptide encoded by a polynucleotide comprising a sequence set forth in
5 Table I;
 - (b) an isolated polypeptide comprising a polypeptide sequence set forth in Table I; and
 - (c) a polypeptide sequence of a gene set forth in Table I.
2. An isolated polynucleotide selected from the group consisting of:
 - 10 (a) an isolated polynucleotide comprising a polynucleotide sequence set forth in Table I;
 - (b) an isolated polynucleotide of a gene set forth in Table I;
 - (c) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide set forth in Table I;
 - (d) an isolated polynucleotide encoding a polypeptide set forth in Table I;
 - 15 (e) a polynucleotide which is an RNA equivalent of the polynucleotide of (a) to (d);
or a polynucleotide sequence complementary to said isolated polynucleotide.
3. An expression vector comprising a polynucleotide capable of producing a polypeptide of
20 claim 1 when said expression vector is present in a compatible host cell.
4. A process for producing a recombinant host cell which comprises the step of introducing
an expression vector comprising a polynucleotide capable of producing a polypeptide of claim
1 into a cell such that the host cell, under appropriate culture conditions, produces said
polypeptide.
25
5. A recombinant host cell produced by the process of claim 6.
6. A membrane of a recombinant host cell of claim 7 expressing said polypeptide.
- 30 7. A process for producing a polypeptide which comprises culturing a host cell of claim 7
under conditions sufficient for the production of said polypeptide and recovering said
polypeptide from the culture.

SEQUENCE LISTING

<110> SMITHKLINE BEECHAM CORPORATION
SMITHKLINE BEECHAM p.l.c.

<120> NOVEL COMPOUNDS

<130> GP50016

<140> TO BE ASSIGNED

<141> 2001-03-05

<150> 60/187,107

<151> 2000-03-06

<150> 60/236,874

<151> 2000-10-03

<150> 60/188,916

<151> 2000-03-13

<150> 60/237,846

<151> 2000-10-03

<160> 52

<170> FastSEQ for Windows Version 3.0

<210> 1

<211> 2301

<212> DNA

<213> Homo sapiens

<400> 1

atggaaaaag ttctttttta tctgtttctc attggcatag cagtgaaagc tcagatctgt	60
ccaaagcggt gtgtctgtca gattttgtct cctaattctg caacccttg tgccaagaaa	120
gggcttttât ttgttcacc aaacattgac agaagaactg tggaactgcg gttggcagac	180
aattttgtta caaatattaa aaggaaagat ttgccaata tgaccagctt ggtggacctg	240
actctatcca ggaatacaat aagttttatt acacctcatg ctttcgctga cctacgaaat	300
ttgagggctt tgcatattgaa tagcaacaga ttgactaaaa ttacaaatga tatgttcagt	360
ggtctttcca atcttcatca tttgatactg aacaacaatc agctgacttt aatttcctct	420


```

acagcgtttg atgatgtctt cgcccttgag gagctggatc tgtcctataa taatctagaa      480
accattcctt gggatgctgt tgagaagatg gttagcttgc atacccttag tttggatcac      540
aatatgattg ataacattcc taaggggacc ttctcccat tgcacaagat gactcggtta      600
gatgtgacat caaataaatt gcagaagcta ccacctgacc ctctctttca gcgagctcag      660
gtactagcaa cctcaggaat cataagccca tctacttttg cattaagttt tgggtgaaac      720
cccttgcaat gcaattgtga attgttgtgg ttgaggcgtc tgtccagaga agatgactta      780
gagacctgtg ctctcctcc acttttaact ggccgctact tttggtcaat tcctgaagaa      840
gagtttttgt gtgagcctcc tctcattact cgtcatacac atgagatgag agtcctggag      900
ggacaaaggg caacactgag gtgcaaagcc aggggagacc ctgagcctgc aattcactgg      960
atctctcctg aagggaagct tatttcaaat gcaacaagat ctctggtgta tgataacgga     1020
acacttgaca ttcttatcac aactgtaaag gatacagggtg cttttacctg cattgcttcc     1080
aatcctgctg gggaagcaac acaaatagtg gatcttcata taattaagct ccctcactta     1140
ctaaatagta caaacatat ccatgagcct gatcctgggtt cttcagatat ctcaacttct     1200
accaagtcag gttctaatac aagcagtagt aatggtgata ctaaattgag tcaagataaa     1260
attgtggttg cagaagctac atcatcaacg gcactactta aatttaattt tcaaagaaat     1320
atccctggaa tacgtatgtt tcaaatccag tacaatggta cttatgatga caccctgtt     1380
tacagaatga tacctcctac gagcaaaact tttctggtca ataactctggc tgctggaact     1440
atgtatgact tgtgtgtctt ggccatatat gatgatggca tcacttccct cactgccaca     1500
agagtctgtg gttgcatcca gtttactacg gaacaggatt atgtgcgttg ccatttcctg     1560
cagtctcagt ttttgggagg caccatgatt attattattg gtggaatcat tgtagcatct     1620
gtgctggtat tcatcattat tctgatgatc cgggtataagg tttgcaacaa taatgggcaa     1680
cacaagggtc ccaagggttag caatgtttat tcccaaacta acgggggtca aatacaaggc     1740
tgtagtgtaa cgctgccccg gtccgtgtcc aaacaagctg tgggacacga agagaatgcc     1800
cagtgttgta aagctaccag tgacaatgtg attcaatctt cagaaacttg ttcgagtcag     1860
gactccteta ccactacctc tgctttgcct ccttctctgga cttcaagcac ttctgtgtcc     1920
caaaagcaga aaagaaagac tggcacaaaag ccaagtacag aaccacagaa tgaagccgtc     1980
acaaatgttg aatcccaaaa cactaacagg aacaactcaa ctgccttgca gttagctagc     2040
cgtcctcccg attctgtcac agaggggccc acgtctaaaa gagcacatat aaagccaagt     2100
aagtttatca ctttgcctgc tgagagatcc ggagcaaggc acaagtactc cctcaatgga     2160
gaattaaagg aatactattg ttatattaac tcgccgaaca catgtggact gtttcctaaa     2220
agaagcatgt ctatgaatgt gatgtttatt cagtctgact gttctgatgg tcatagtgga     2280
aaggcaactc tcaaattctg a                                     2301

```

<210> 2

<211> 445

<212> DNA

<213> Homo sapiens

<400> 2

```

aatgctgggc ctgccgtgga agggaggtct gtccctgggcg ctgctgctgc ttctcttagg      60
ctcccgatc ctgctgatct atgcctggca tttccacgag caaagggact gtgatgaaca      120
caatgtcatg gctcggtacc tcctgccac agtggagttt gctgtccaca cattcaacca      180

```

acagagcaag gactactatg cctacagact ggggcacatc ttgaattcct ggaaggagca	240
ggtggagtcc aagactgtat tctcaatgga gctactgctg gggagaacta ggtgtgggaa	300
atttgaagac gacattgaca actgccatth ccaagaaagc acagagctga acaatacttt	360
cacctgcttc ttcacatca gcaccaggcc ctggatgact cagttcagcc tcctgaacaa	420
gacctgcttg gagggattcc actga	445

<210> 3

<211> 477

<212> DNA

<213> Homo sapiens

<400> 3

atgtggagtc tgccgccgag cagggctctg tcctgtgctg cactgctgct tctcttcagc	60
ttccagttcc tggttacctg tgcttggcgt ttccaagagg aagaggagtg gaatgaccaa	120
aaacaaattg ctgtttatct cctccacc ctggagtttg cctgttacac attcaacaag	180
cagagcaagg actggtatgc ctacaagctg gtgcctgtcc tggcttcctg gaaggagcag	240
ggttatgata agatgacatt ctccatgaat ctgcaactgg gcagaaccat gtgtgggaaa	300
tttgaagatg acattgacaa ctgccctttt caagagagcc cagagctgaa caatgtaaga	360
caagacacca gcttccctcc tggatacagc tgtggatgcc gcattgggtg tgggtcggac	420
acagacctgc acctgcttct tcaccattgg aatagagccc tggaggacac ggtttga	477

<210> 4

<211> 444

<212> DNA

<213> Homo sapiens

<400> 4

atgtggagtc tgccgccgag cagggctctg tcctgtgctg cactgctgct tctcttcagc	60
ttccagttcc tggttacctg tgcttggcgt ttccaagagg aagaggagtg gaatgaccaa	120
aaacaaattg ctgtttatct cctccacc ctggagtttg cctgttacac attcaacaag	180
cagagcaagg actggtatgc ctacaagctg gtgcctgtcc tggcttcctg gaaggagcag	240
ggttatgata agatgacatt ctccatgaat ctgcaactgg gcagaaccat gtgtgggaaa	300
tttgaagatg acattgacaa ctgccctttt caagagagcc cagagctgaa caatacctgc	360
acctgcttct tcaccattgg aatagagccc tggaggacac ggtttgacct ctggaacaag	420
acgtgctcag gcgggcattc ctga	444

<210> 5

<211> 2463

<212> DNA

<213> Homo sapiens

<400> 5

atgctgcgcc	tggggctgtg	cgggggggcg	ctgctgtgcg	tgtgccggcc	gggtgccgtg	60
cgtgccgact	gctggctcat	tgagggcgac	aagggctacg	tgtggctggc	catctgcagc	120
cagaaccagc	cgccctacga	gaccatcccc	cagcacatca	atagcaccgt	gcacgacctg	180
cggctcaacg	agaacaagct	caaagccgtg	ctctactcct	cgctcaaccg	ctttgggaac	240
ctcaccgacc	tcaacctcac	caagaacgag	atctcctaca	tcgaggacgg	tgccttcctg	300
ggccagtcga	gcctgcaggt	cctgcagctg	ggctacaaca	agctcagcaa	cctgacggag	360
ggcatgctgc	gaggcatgag	ccgcctgcag	ttcctctttg	tccagcacia	cctcatcgag	420
gtggtgacgc	ccaccgcctt	ctccgagtg	ccgagcctca	tcagcatcga	cctgtcctcc	480
aaccgcctca	gccgcctgga	cgggtgccacc	tttgccagcc	tcgccagcct	gatggtgtgt	540
gagctggccg	gcaacccctt	caactgtgag	tgcgacctct	tcggcttcct	ggcctggctg	600
gtggtcttca	acaacgtcac	caagaactac	gaccgcctgc	agtgtgagtc	gccgcgggag	660
tttgccggct	accgcgtgct	ggtgccccgg	ccctaccaca	gcctcaacgc	catcaccgta	720
ctccaggcca	agtgtcggaa	tggtctcgctg	cccgcccggc	ccgtgagcca	ccccacgccc	780
tactccaccg	acgcccagag	ggagccagac	gagaactcgg	gcttcaaccc	cgacgagatc	840
ctttcggttg	agccgcgggc	ctcgccacc	acggatgcgt	cggcagggcc	agccatcaag	900
ctgcaccacg	tcacgttcac	ctcgccacc	ctggtggtca	tcacccaca	cccctacagc	960
aagatgtaca	tcctcgtgca	gtacaacaac	agctacttct	ccgacgtcat	gacctcaag	1020
aacaagaagg	agatcgtgac	gctggacaaa	ctgcggggcg	acactgagta	caccttctgc	1080
gtgacctcgc	tgcgcaacag	ccgcgccttc	aaccacacct	gcctgacctt	caccacgcgg	1140
gaccccgctc	ccggagactt	ggcgcccagc	acctccacca	ccacccacta	catcatgacc	1200
atcctgggct	gcctcttttg	catggttatc	gtgctgggag	ccgtgtacta	ctgcctgcgc	1260
aagcggcgca	tgcaggagga	gaagcagaag	tctgtcaacg	tcaagaagac	catcctggag	1320
atgcgctacg	gggctgatgt	ggatgccggc	tccattgtgc	acgcgcacca	gaagctgggc	1380
gagcctcccg	tgtgcccgt	atctcgcatg	gcctccatcc	cctccatgat	cggggagaag	1440
ctgcccaccg	ccaaggggtt	ggaggccggg	ctggacacac	ccaaggtagc	caccaaaggc	1500
aactatatcg	aggtgcgcac	aggcgccggc	ggggacggtc	tggctcggcc	cgaggatgac	1560
ctcccggaac	tcgagaacgg	ccagggtctg	gctgcagaga	tctccaccat	tgccaaggag	1620
gtggacaagg	tcaaccagat	cattaacaac	tgcatcgatg	ctctcaagct	ggactcggcc	1680
tcttttcttg	gaggcggcag	cagcagtggg	gaccccgagc	tggccttcga	gtgccagtcc	1740
ctccctgcag	ctgctgccgc	ctcctcagcc	actggccccg	gggccttggg	gcggcccagc	1800
ttcctttcgc	ctccctacaa	ggagagctcc	caccacccac	tacagcgcca	gctgagcgcc	1860
gacgcggccg	tgaccgcgaa	gacctgcagc	gtgtcgtcca	gtggttccat	caagagcgcc	1920
aaggctctta	gcctggacgt	gcccagccat	ccggcgcca	cagggtggc	taaggcgac	1980
tccaagtaca	tcgagaaggg	cagccccctc	aacagccgcg	tggaccggct	cccgtggtg	2040
ccggcgggca	gcggcggggg	cagcggcggg	ggcgggggca	tccaccacct	ggagggtgaag	2100
ccggcctacc	actgcagcga	gcaccggcac	agctttcccg	ccctgtacta	cgaggagggt	2160
gccgacagcc	tgagccagcg	cgtgtccttc	ctcaagccgc	tgaccgcctc	caagcgtgac	2220
tccacctact	cgcagctctc	ccccagacac	tactactcag	ggtactcctc	cagcccagag	2280
tactcatccg	agagcacgca	caagatctgg	gagcgcttcc	ggccctacaa	gaagcaccac	2340
cgggaggagg	tgtacatggc	cgcgggtcac	gccctgcgca	agaaggcca	gttcgccaag	2400
gacgaggatc	tgcattgacat	ccttgattac	tgggaagggg	tctccgcca	gcagaagctg	2460
tga						2463

<210> 6

<211> 2601

<212> DNA

<213> Homo sapiens

<400> 6

```

atgaccattg aaaaaatgtt ttctttttat ttttttagatt atttctcttt attcagaagc      60
atacagttgt ttgctgattg caagaagatg tttctgtggc tgtttctgat tttgtcagcc      120
ctgatttctt cgacaaatgc agattctgac atatcgggtg aaatttgcaa tgtgtgttcc      180
tgcgtgtcag ttgagaatgt gctctatgtc aactgtgaga aggtttcagt ctacagacca      240
aatcagctga aaccaccttg gtctaatttt tatcacctca atttccaaaa taatttttta      300
aatattctgt atccaaatac attcttgaat ttttcacatg cagtctccct gcatctgggg      360
aataataaac tgcagaacat tgagggagga gcctttcttg ggctcagtgc attaaagcag      420
ttgcacttga acaacaatga attaaagatt ctccgagctg acactttcct tggcatagag      480
aacttggagt atctccaggc tgactacaat ttaatcaagt atattgaacg aggagccttc      540
aataagctcc acaaactgaa agttctcatt cttaatgaca atctgatttc attccttcct      600
gataatattt tccgattcgc atctttgacc catctggata tacgagggaa cagaatccag      660
aagctccctt atatcggggg tctggaacac attggccgtg tcgttgaatt gcaactggaa      720
gataaccctt ggaactgtag ctgtgattta ttgcccttaa aagcttggct ggagaacatg      780
ccatataaca ttacatagg agaagctatc tgtgaaactc ccagtgactt atatggaagg      840
cttttaaaag aaaccaacaa acaagagcta tgtcccatgg gcaccggcag tgattttgac      900
gtgcgcatcc tgectccatc tcagctggaa aatggctaca ccactcccaa tggtcacact      960
acccaaacat ctttacacag attagtaact aaaccaccaa aaacaacaaa tccttccaag     1020
atctctggaa tcgttgcagg caaagccctc tccaaccgca atctcagtca gattgtgtct     1080
taccaaacaa ggggtgctcc tctaacacct tgcccggcac cttgcttctg caaaacacac     1140
ccttcagatt tgggactaag tgtgaactgc caagagaaaa atatacagtc tatgtctgaa     1200
ctgataccga aaccttttaa tgcaagaag ctgcacgtca atggcaatag catcaaggat     1260
gtggacgtat cagacttcac tgactttgaa ggactggatt tgcttcattt aggcagcaat     1320
caaattacag tgattaaggg agacgtattt cacaatctca ctaatttacg caggctatat     1380
ctcaatggca atcaaattga gagactctat cctgaaatat tttcagggtc tcataacctg     1440
cagtatctgt atttggaata caatttgatt aaggaaatct cagcaggcac ctttgactcc     1500
atgccaaatt tgcagttact gtacttaaac aataatctcc taaagagcct gcctgtttac     1560
atcttttccg gagcacctt agctagactg aacctgagga acaacaaatt catgtacctg     1620
cctgtcagtg gggtccttga tcagttgcaa tctcttacac agattgactt ggagggcaac     1680
ccatgggact gtacttgtga cttgggtggca ttaaagctgt ggggtggagaa gttgagcgac     1740
gggattgttg tgaaagaact gaaatgtgag acgcctgttc agtttgcaa cattgaactg     1800
aagtccctca aaaatgaaat cttatgtccc aaacttttaa ataagccgtc tgcaccatc     1860
acaagccctg cacctgccat tacattcacc actccttttg gtcccatctg aagtccctc     1920
gggtggccag tgectctgtc tattttaatc ttaagtatct tagtggtcct cattttaacg     1980
gtgtttgttg ctttttgctt tcttgttttt gtctgcgcac gcaacaagaa acccacagtg     2040
aagcacgaag gcctggggaa tcctgactgt ggctccatgc agctgcagct aaggaagcat     2100

```

gaccacaaaa	ccaataaaaa	agatggactg	agcacagaag	ctttcattcc	acaaactata	2160
gaacagatga	gcaagagcca	cacttggtggc	ttgaaagagt	cagaaactgg	gttcattgtt	2220
tcagatcctc	caggacagaa	agttgttatg	agaaatgtgg	ccgacaagga	gaaagattta	2280
ttacatgtag	ataccaggaa	gagactgagc	acaattgatg	agctggatga	attattccct	2340
agcagggatt	ccaatgtgtt	tattcagaat	tttcttgaaa	gcaaaaagga	gtataatagc	2400
ataggtgtca	gtggctttga	gatccgctat	ccagaaaaac	aaccagacaa	aaaaagtaag	2460
aagtactga	taggtggcaa	ccacagtaaa	attgttgtgg	aacaaaggaa	gagtgagtat	2520
tttgaactga	aggcgaaact	gcagagttcc	cctgactacc	tacaggtcct	tgaggagcaa	2580
acagctttga	acaagatcta	g				2601

<210> 7

<211> 1602

<212> DNA

<213> Homo sapiens

<400> 7

atggctccag	gacccttctc	ctcgccctc	ctctcgccgc	cgcccgctgc	cctgcccttt	60
ctgctgctgc	tctgggctgg	ggcatctcgt	ggccagccct	gccccggccg	ctgcatctgc	120
cagaacgtgg	cgccacact	gacaatgctg	tgcgccaaag	ccggcttget	ctttgtgccg	180
cccgccatcg	accggcgctg	ggtggagctg	cggtccaccg	acaacttcac	cgccgctgtg	240
cgccgctgag	acttcgcca	catgaccagc	ctggtgcacc	tcactctctc	ccggaacacc	300
atcgccagg	tggcagctgg	cgcttcgcc	gacctgcgtg	ccctccgggc	cctgcacctg	360
gacagcaacc	gcctggcgga	ggtgcgcggc	gaccagctcc	gcggcctggg	caacctccgc	420
cacctgatcc	ttggaacaa	ccagatccgc	cggttgaggt	cgccgctctt	tgacgccttc	480
ctgtccaccg	tggaggacct	ggatctgtcc	tacaacaacc	tggaggccct	gccgtgggag	540
gcggtgggcc	agatggtgaa	cctaaacacc	ctcacgctgg	accacaacct	catcgaccac	600
atcgcgagg	ggaccttcgt	gcagcttcac	aagctgggtc	gtctggacat	gacctccaac	660
cgctgcata	aactcccgcc	cgacgggctc	ttcttgaggt	cgcagggcac	cgggcccaag	720
ccgccaccc	cgctgaccgt	cagcttcggc	ggcaaccccc	tgactgcaa	ctgcgagctg	780
ctctggctgc	ggcggtgac	ccgcgaggac	gacttagaga	cctgcgccac	gcccgaacac	840
ctcaccgacc	gctacttctg	gtccatcccc	gaggaggagt	tcctgtgtga	gccccgctg	900
atcacacggc	aggcgggggg	ccgggcccctg	gtggtggaag	gccaggcggt	gagcctgcgc	960
tgccgagcgg	tgggtgacct	cgagccgggtg	gtgcactggg	tggcacctga	tggcggtgtg	1020
ctggggaact	ccagccggac	ccgggtccgg	ggggacggga	cgctggatgt	gaccatcacc	1080
accttgaggg	acagtggcac	cttcacttgt	atcgccctca	atgctgctgg	ggaagcgacg	1140
gcgcccgtgg	aggtgtgctg	ggtacctctg	cctctgatgg	cacccccgcc	ggctgccccg	1200
ccgctctca	ccgagcccg	ctcctctgac	atcgccacgc	cgggcagacc	aggtgccaac	1260
gattctgcgg	ctgagcgctg	gctcgtggca	gccgagctca	cctcgaactc	cgtgctcatc	1320
cgctggccag	cccagaggcc	tgtgcccggg	atagcatgt	accaggttca	gtacaacagt	1380
tccgttgatg	actccctcgt	ctacagctct	gcctccctca	tgacatttgt	agagcaccag	1440
ttaaatgctt	cagtcactctg	cttggttca	cctggagatg	ccagcggggc	tggagctgtt	1500
tccctacctg	tggagagcct	cagctcctgg	ctgtcagatc	ttcaccgaga	aacctgcctc	1560

ttggcctcca tctctgcctt tccagtgttt tcttgccat ag

1602

<210> 8

<211> 2316

<212> DNA

<213> Homo sapiens

<400> 8

atggctccag gacccttctc ctggccctc ctctgcgcg cgcccgctgc cctgccttt	60
ctgtgtctgc tctggcggg ggcattctgt ggccagccct gcccggcg ctgcattctgc	120
cagaacgtgg cgccacact gacaatgctg tgcgccaaga ccggttgct ctttgtgccg	180
cccgccatcg accggcgct ggtggagctg cggtcaccg acaacttcat cgccgctg	240
cgccgctgag acttcgcaa catgaccagc ctggtgcacc tactctctc ccggaacacc	300
atcgccagg tggcagctgg cgccttcgcc gacctgcgtg ccctccggc cctgcacctg	360
gacagcaacc gcctggcgga ggtgcgcggc gaccagctcc gggcctggg caacctccgc	420
cacctgatcc ttggaacaa ccagatccgc cgggtggagt cggcgccct tgcgccttc	480
ctgtccaccg tggaggacct ggatctgtcc tacaacaac tggaggccct gccgtgggag	540
gcggtgggccc agatggtgaa cctaaacacc ctacgctgg accacaacct catcgaccac	600
atcgcgagg ggaccttctg gcagcttcac aagctggctc gtctggacat gacctccaac	660
cgctgcata aactccgcc cgacgggctc ttctgaggt cgagggcac cgggccaag	720
ccgccaccc cgctgaccgt cagcttcggc ggcaacccc tgactgcaa ctgcgagctg	780
ctctggctgc ggcggctgac ccgcgaggac gacttagaga cctgcgccac gccgaacac	840
ctcaccgacc gctacttctg gtccatcccc gaggaggagt tctgtgtga gccccgctg	900
atcacacggc agggcggggg ccgggcctg gtggtggaag gccaggcggg gaggctgcgc	960
tgcgagcgg tgggtgacct cgagcgggtg gtgactggg tggcacctga tggcggtg	1020
ctggggaact ccagccggac ccgggtccgg ggggacggga cgctggatgt gaccatcacc	1080
accttgaggg acagtggcac ctacttctg atcgctcca atgtgtctg ggaagcgacg	1140
gcgcccgctg aggtgtgct ggtacctctg cctctgatgg ccccccgcc ggctgccccg	1200
ccgctctca ccgagcccg ctcctctgac atcgccacgc cgggcagacc aggtgccaac	1260
gattctgctg ctgagcgtc gctcgtggca gccgagctca cctcgaacte cgtgctcatc	1320
cgctggccag ccagaggcc tgtgcccgga atacgcatgt accaggttca gtacaacagt	1380
tccgttgatg actccctctg ctacaggatg atcccgcca ccagtcagac cttcctggtg	1440
aatgacctgg cggcgggcg tgcctacgac ttgtgcgtgc tggcggtcta cgacgacggg	1500
gccacagcgc tgcgggcaac gcgagtggg ggctgtgtac agttcaccac cgctggggat	1560
ccggcgccct gccgccgct gagggcccat ttctggggc gcacatgat catcgccatc	1620
gggggctgca tgcctgcctc ggtcctcgtc ttcacgttc tgctcatgat ccgctataag	1680
gtgtatggcg acggggacag ccgccgctc aagggtcca ggtcgctccc gcgggtcagc	1740
cacgtgtgct cgcagaccaa cggcgccagg acaggcgcg cacaggcccc ggccctgccg	1800
gccaggacc actacgaggc gctgcgcgag gtggagtccc aggtgcccc cgccgtcgcc	1860
gtcagggcca aggccatgga ggccgagac gcaccccgcg agccggaggg ggtccttgga	1920
cgttctctgg gcggctcggc cacctcgtg tgctgtctgc catccgagga aacttcggg	1980
gaggagtctc gggcgcggt gggccctcga aggagccgat cggcgccct ggagccacca	2040

acctcggcgc	cccctactct	agctctagtt	cctgggggag	ccgcggcccg	gccgaggccg	2100
cagcagcgct	attcgttcga	cggggactac	ggggcactat	tccagagcca	cagttacccg	2160
cgccgcgccc	ggcggacaaa	gcgccaccgg	tccacgcccg	acctggacgg	ggctggaggg	2220
ggcgcgcccg	gggaggatgg	agacctgggg	ctgggctccg	ccagggcgctg	cctggctttc	2280
accagcaccg	agtggatgct	ggagagtacc	gtgtga			2316

<210> 9

<211> 1200

<212> DNA

<213> Homo sapiens

<400> 9

atgtggcagc	ttttagcagc	agcatgctgg	atgcttcttc	ttggatctat	gtatggttat	60
gacaagaaag	gaaacaatgc	aaaccctgaa	gctaatatga	atattagcca	gattatttct	120
tactgggggt	atccttatga	agagtatgat	gttacacaaa	aagatggtta	tatccttgga	180
atttatagga	ttccacatgg	aagaggatgc	ccagggagga	cagctccaaa	gcctgctgtg	240
tatttgacgc	atggcttaat	tgcatctgcc	agtaactgga	tttgcaacct	gccaacaac	300
agtttggtt	tccttctggc	agatagtgg	tatgacgtgt	ggttggggaa	cagccgagga	360
aacacttgg	ccagaaaaca	ccttaaattg	tcaccgaaat	caccagaata	ctgggccttc	420
agtttggtg	agatggctaa	atatgacctt	ccagccacaa	tcaattttat	catagagaaa	480
actggacaga	agcgactcta	ctacgtgggc	cactcacaag	gcaccacat	agcttttata	540
gcattttcta	caaaccacga	actggctaaa	aagattaaga	tattttttgc	actggctcca	600
gttgctcacg	ttaaatacac	caaagtcc	atgaaaaaac	taacaaccct	ttccaggcga	660
gtagttaagg	tggtgtttgg	tgacaaaatg	ttccaccctc	atacattgtt	tgaccaattc	720
attgccacca	aagtgtgcaa	tcgaaagcta	ttccgtcgta	tttgacgcaa	cttcctattt	780
actctgagtg	gatttgatcc	gcaaaactta	aatatgagtc	gcttggatgt	ttatttgtca	840
cacaatcctg	cgggaacatc	tggtcagaat	atgctgcact	gggtcaggc	tgtaattct	900
ggtcagctcc	aagcttttga	ttggggaaac	tctgatcaga	acatgatgca	cttcaccag	960
cttacacctc	ctttatacaa	cattactaag	atcgaagttc	caacagcaat	atggaatggt	1020
ggacaggaca	ttgtggctga	tcccaggat	gttgaaaatt	tacttcctca	aattgctaac	1080
cttatttatt	acaagctgat	tccacactac	aatcatgtgg	atttttacct	tggagaggat	1140
gcacctcagg	aaatttacca	agacctaat	atattgatgg	aagaatattt	acaaaattaa	1200

<210> 10

<211> 768

<212> DNA

<213> Homo sapiens

<400> 10

atcgtggggg	gctcaaacgc	gcagccgggc	acctggcctt	ggcaagtgg	cctgcaccat	60
ggaggtggcc	acatctgcgg	gggtccctc	atcgccccct	cctgggtcct	ctccgctgct	120
cactgtttca	tgacggggcg	gcagtaccgc	tgcccgga	cccgcgcac	gcgctctgcc	180

```

ctgcctacca ggaaaaggag gagggcctat aaccactaca gccagggctc agacctggcc      240
ctgctgcagc tcgcccaccc caccgcccac acacccctct gcctgcccc a gcccgcccat      300
cgcttccctt ttggagcctc ctgctgggcc actggctggg atcaggacac cagtgatgcc      360
ccgtctcttt caccagctcc tgggacccta cgcaatctgc gcctgcgtct catcagtcgc      420
cccacatgta actgtatcta caaccagctg caccagcgac acctgtccaa cccggcccgg      480
cctgggatgc tatgtggggg cccccagcct ggggtgcagg gcccctgtca gggcttgttt      540
ggggcaccac tgggtgcatga ggtgaggggc acatggttcc tggccgggct gcacagtttc      600
ggagatgctt gccaaggccc cgcagggccg gcggtcttca ccgcgctccc tgctatgagg      660
actgggtcag cagtttggac tcggcaggtc tacttcgccg aggaaccaga gcccagagct      720
gagcctggaa gctgcctggc caacataaga ccttctctc tccagtga      768

```

<210> 11

<211> 906

<212> DNA

<213> Homo sapiens

<400> 11

```

atggagactg ctgggagtga ttgggttgca ggaggcccac tgaccagggc ctctcacccc      60
tcagagtgcg ggaaggcccc gcggccaggg gcctggccct gggaggccca ggtgatggtg      120
ccaggatcca gacctgcca tggggcgctg gtgtctgaaa gctgggtctt ggcacctgcc      180
agctgctttc tggagcaagt aacacacaca ctttgttgct gcagaatgac tcgcgttggg      240
gccttttgtg ccaggaggag gggacctggg ttctggctgg aatcagagac tttcccagtg      300
gctgtctact tgcccagggc ctataaccac tacagccagg gctcagacct ggccctgctg      360
cagctcgccc accccacgac ccacacaccc ctctgcctgc cccagcccgc ccatcgcttc      420
ccctttggag cctcctgctg ggccactggc tgggatcagg acaccagtga tgctcctggg      480
accctaagca atctgcgcct gcgtctcatc agtcgcccc catgtaactg tatctacaac      540
cagctgcacc agcgacacct gtccaaccgg gcccggcctg ggatgctatg tgggggcccc      600
cagcctgggg tgcagggcc ctgtcagggc ttgtttgggg caccactggt gcatgaggtg      660
aggggcacat ggttcctggc cgggctgcac agtttcggag atgcttgcca aggccccgcc      720
aggccggcgg tcttcaccgc gctccctgct atgaggactg ggtcagcagt ttggactcgg      780
caggtctact tcgccgagga accagagccc gaggtgagc ctggaagctg cctggccaac      840
ataagtatgt ggccccgggg cctcctgcca aacctgcct ctccaggacc cttctctctc      900
cagtga      906

```

<210> 12

<211> 1152

<212> DNA

<213> Homo sapiens

<400> 12

```

atgcccagcg gctgccgctg cctgcatctc gtgtgcctgt tgtgcattct gggggctccc      60
ggtcagcctg tccgagccga tgactgcagc tcccactgtg acctggccca cggctgctgt      120

```



```

gcacctgacg gctcctgcag gtgtgacccg ggctgggagg ggctgcactg tgagcgctgt 180
gtgaggatgc ctggctgcc a gcacgggtacc tgccaccagc catggcagtg catctgccac 240
agtggctggg caggcaagtt ctgtgacaaa gatgaacata tctgtaccac gcagtecccc 300
tgccagaatg gaggccagtg catgtatgac gggggcggtg agtaccattg tgtgtgctta 360
ccaggettcc atgggcgtga ctgcgagcgc aaggctggac cctgtgaaca ggcaggctcc 420
ccatgccgca atggcgggca gtgccaggac gaccagggtt ttgctctcaa cttcacgtgc 480
cgctgcttgg tgggctttgt gggtgccgc tgtgaggtaa atgtggatga ctgcctgatg 540
cggccttgtg ctaacgggtg cacctgcctt gacggcataa accgcttctc ctgcctctgt 600
cctgagggct ttgctggacg cttctgcacc atcaacctgg atgactgtgc cagccgcca 660
tgccagagag gggcccgtg tcgggacgt gtccatgact tcgactgcct ctgccccagt 720
ggctatggtg gcaagacttg tgagcttgtc ttacctgtcc cagaccccc aaccacagtg 780
gacacccctc tagggccac ctcagctgta gtggtacctg ccacggggcc agccccccac 840
agcgcagggg ctggtctgct gcggtctca gtgaaggagg tggtgcgag gcaagaggct 900
gggctaggtg agcctagctt ggtggccctg gtggtgtttg gggccctcac tgctgcctg 960
gttctggcta ctgtgttgc gacctgagg gcctggcgcc ggggtgtctg ccccttgga 1020
ccctgttgc accctgcccc aactatgct ccagcgtgcc aggaccagga gtgtcaggtt 1080
agcatgctgc cagcagggt cccctgcc cgtgacttgc cccctgagcc tggaaagacc 1140
acagcactgt ga 1152

```

<210> 13

<211> 1254

<212> DNA

<213> Homo sapiens

<400> 13

```

atggcatctt acctttatgg agtactcttt gctgttgcc tctgtgtctc aatctactgt 60
gtgtccccgg ccaatgcccc cagtgcatac cccgcctt cctccacaaa gagcaccct 120
gcctcacagg tgtattccct caacaccgac tttgccttcc gcctataccg caggctgggt 180
ttggagacct cgagtcagaa catcttcttc tccccgtga gtgtctccac ttccctggcc 240
atgtctctcc ttggggccca ctcagtcacc aagaccaga ttctccaggg cctgggcttc 300
aacctcacac acacaccaga gtctgccatc caccagggt tccagcacct ggttcaactc 360
ctgactgttc ccagcaaaga cctgaccttg aagatgggaa gtgcctctt cgtcaagaag 420
gagctgcagc tgcaggcaaa tttcttgggc aatgtcaaga ggctgtatga agcagaagtc 480
ttttctacag atttctccaa cccctccatt gccaggcga ggatcaacag ccattgtgaa 540
aagaagacct aagggaaggt ttagacata atccaaggcc ttgaccttct gacggccatg 600
gttctgggtg accacatctt ctttaaagcc aagtgggaga agccctttca ccctgaatat 660
acaagaaaga acttccatt cctgggtggc gagcagggtc ctgtgcatgt ccccatgatg 720
caccagaaag agcagttcgc ttttgggtg gatacagagc tgaactgctt tgtgctgcag 780
atggattaca agggagatgc cgtggccttc tttgtctcc ctagcaaggg caagatgagg 840
caactggaac aggccttgtc agccagaaca ctgagaaagt ggagccactc actccagaaa 900
aggtggatag aggtgttcat cccagattt tccatttctg cctcctacaa tctggaaacc 960
atcctccga agatgggcat ccaaatgtc tttgacaaa atgctgattt ttctggaatt 1020

```

gcaaagagag	actccctgca	ggtttctaaa	gcaaccacaca	aggctgtgct	ggatgtcagt	1080
gaagagggca	ctgaggccac	agcagctacc	accaccaagt	tcatagtccg	atcgaaggat	1140
ggccctctt	acttcactgt	ctccttcaat	aggaccttcc	tgatgatgat	tacaaataaa	1200
gccacagacg	gtattctctt	tctagggaaa	gtggaaaatc	ccactaaatc	ctag	1254

<210> 14

<211> 732

<212> DNA

<213> Homo sapiens

<400> 14

atgggggtcca	gcagcttctt	gttcctcatg	gtgtctctcg	ttcttgtgac	cctgggtggct	60
gtggaaggag	ttaaagaggg	tatagagaaa	gcaggggttt	gccagctga	caacgtacgc	120
tgcttcaagt	ccgatcctcc	ccagtgtcac	acagaccagg	actgtctggg	ggaaaggaag	180
tggtgttacc	tgcactgtgg	cttcaagtgt	gtgattcctg	tgaaggaact	ggaagaagg	240
cagcgcttat	tacataaccg	tgagcttcct	ccagctgcaa	tattaggaga	ttctcttaca	300
gagaaatcgg	ggggctgccc	gccagatgat	gggccctgcc	tcctatcggg	gcctgaccag	360
tgctgtggaag	acagccagtg	tcccttgacc	aggaagtgtc	gctacagagc	ttgcttccgc	420
cagtgtgtcc	ccaggggtctc	tggtaaatgc	ctccctcca	ccttgtctgac	catccaagcc	480
ccaagcttca	gggccagtg	gcaaggacgg	agctcaccca	gttccctgtg	ttgcagtga	540
gctgggcagc	tgcccagagg	accaactgcg	ctgcctcagc	cccatgaacc	acctgtgtca	600
caaggactca	gactgtctcg	gcaaaaagcg	atgctgccac	agcgctgctg	ggcgggattg	660
ccgggatcct	gccagaggta	cggctcctgg	gtgcccagg	caggtgcctc	ccctctccga	720
gccagctct	aa					732

<210> 15

<211> 558

<212> DNA

<213> Homo sapiens

<400> 15

atgggggtcca	gcagcttctt	gttcctcatg	gtgtctctcg	ttcttgtgac	cctgggtggct	60
gtggaaggag	ttaaagaggg	tatagagaaa	gcaggggttt	gccagctga	caacgtacgc	120
tgcttcaagt	ccgatcctcc	ccagtgtcac	acagaccagg	actgtctggg	ggaaaggaag	180
tggtgttacc	tgcactgtgg	cttcaagtgt	gtgattcctg	tgaaggaact	ggaagaagtt	240
ccctgtgttg	cagtgaagct	gggcagctgc	ccagaggacc	aactgcgctg	cctcagcccc	300
atgaaccacc	tgtgtcacia	ggactcagac	tgctcgggca	aaaagcgatg	ctgccacagc	360
gcctgcgggc	gggattgccc	ggatcctgcc	agaggtagcg	ctcctgggtg	cccagggcag	420
tgccctcccc	tctccgagcc	cagctcta	actttcttca	ttgctacaag	cttaacagga	480
tgccctcccc	gaagtcagga	cctcccatgg	ccaggattag	gaaactggat	aggggttgga	540
ggagtcctgc	taggatga					558

<210> 16
 <211> 597
 <212> DNA
 <213> Homo sapiens

<400> 16

atgaactcgg gacgcgagcc ccgaacaccc cggacactct taagcatcgc agacatccta	60
gccccgcgca tggccccccg agcaccctct gcgcgcgagc ttccagagtc gggtcggggt	120
ccaacgtcgc cgctgtgcgc gctggaggag ctgactagta aaactttccg cggacttgac	180
gcgcgcgctc tgcagccctc tgaagggcgg gcaggtccgg acgcgctggg ccctgggtccc	240
ttcggccgca aacggcgcaa gtcacgcact gcgttcaccg cgcaacaggt gctggagctg	300
gagcggcgct tcgtcttcca gaagtacctg gcgcgcgtcc agcgagacgg gctagctacg	360
cgactcggcc tggccaacgc gcaggtggtc acttggttcc agaaccggcg agccaagctc	420
aagcgcgatg tggaggagat gcgcgcgcac gtgcgcctgc tacgcgcgtt gtccccggaa	480
gtctctgtca gcttagcact gccgaaggc gctccagatc ccggcctctg cctcggccct	540
gccggccctg actcccggcc ccacctgtca gacgaggaga tacaggtgga cgattga	597

<210> 17
 <211> 993
 <212> DNA
 <213> Homo sapiens

<400> 17

atggtatgga aaagagagaa tttctacaag gaggtcaagc gaggaagagc tttgttttta	60
aaaaggcttt gtattttcaa tattgatact gataatacat ttcaaaggat cattgaaaaa	120
ccatcctggt tgggattttt aggtccaatg attaaagcag agactggaga cttcatttat	180
gtacatgtaa aaaataatgc ttcaagagct tatagttatc atcctcatgg gctcacctac	240
tccaaagaaa atgaaggtgc tatctatcct gataatacga caggcctgca aaaggaagat	300
gaatatctgg agccagggaa acaatatacc tacaagtggg atgtagaaga acatcaggga	360
cctggcccca atgacagtaa ttgtgtgaca agaatttacc attcccatat agacactgca	420
agagatgtag cttcgggact tattggacca atactgactt gtaaaagagc aataaatgga	480
tacatctatg gaaatctgcc caatctcacc atgtgtgctg aagatagggt ccagtgggat	540
tttgttggca tgggtggcgt ggctgacata caccctgtct acctccgagg acaaactctg	600
atctctcgga atcacagaaa ggacaccatt atgctcttcc cctcctcact ggaagatgcc	660
ttcatggtgg ccaaggcccc tggagtgtgg atgctgggat gccagataca tggtagtgat	720
atattacttt tgcgtgatac aaagtcagag aacttccaag ggcttagccc attccacatg	780
catttcctta caaatgaaga gacctatctc caagaagaga gtatgcaggc atttttcaaa	840
gtaagtaatt gccagaaacc ttcaacagaa gcctttgtta ctgggacaca tggtatacat	900
tactatattg ctgctaaaga aattctttgg aactatgctc catctgggat agatttcttc	960
actaaaaaaaa atttaacagc agctggaagg taa	993

<210> 18

<211> 1440

<212> DNA

<213> Homo sapiens

<400> 18

```
atggccatcc tcccgttget cctgtgcctg ctgccgctgg cccctgcctc atccccaccc 60
cagtcagcca caccagccc atgtcccgc cgctgccgt gccagacaca gtcgtgccc 120
ctaagcgtgc tgtgcccagg ggcaggcctc ctgttcgtgc caccctcgct ggaccgccgg 180
gcagccgagc tgcggctggc agacaacttc atcgctccg tgcgccgcg cgacctggcc 240
aacatgacag gcctgctgca tctgagcctg tcgcggaaca ccatccgcca cgtggctgcc 300
ggcgccctcg ccgacctgcg ggcctgcgt gccctgcacc tggatggcaa ccggtgacc 360
tactgggagc agggccagct gcgcggcctg gtcaacttgc gccacctcat cctcagcaac 420
aaccagctgg cagcgtggc ggccggcgcc ctggatgatt gtgccgagac actggaggac 480
ctcgacctct cctacaaca cctcgagcag ctgccctggg aggcctggg ccgctgggc 540
aacgtcaaca cgttgggcct cgaccacaac ctgttggtt ctgtgccgc cggcgctttt 600
tccgcctgc acaagctggc ccggtggac atgacctcca accgcctgac cacaatccca 660
cccgaccac tcttctccg cctgcccctg ctgccaggc cccggggctc gcccgctct 720
gccctggtgc tggcctttgg cgggaacccc ctgactgca actgcgagct ggtgtggctg 780
cgtcgcctgg cgcgggagga cgacctcgag gcctgcgct cccacctgc tctggcggc 840
cgctacttct gggcggtggg cgaggaggag tttgtctgc agccgccctg ggtgactcac 900
cgctcaccac ctctggtgt gcccgaggt cggccggctg cctgcgctg ccgggcagtg 960
ggggacccag agccccgtgt gcgttgggtg taccaccagg gccgctgct aggcaactca 1020
agccgtgccc gcgccttccc caatgggagc ctggagctgc tggtcaccga gccgggtgat 1080
ggtggcatct tcacctgat tgcggccaat gcagctggc aggccacagc tgctgtggag 1140
ctgactgtgg gtccccacc acctcctcag ctagccaaca gcaccagctg tgaccccccg 1200
cgggacgggg atctgatgc tctacccca ccctccgtg cctctgctt tgccaagggtg 1260
gccgacactg ggccccctac cgacctggc gtccagggtg ctgagcacgg ggccacagct 1320
gctcttgtcc agtgccgga tcagcggcct atcccgggca tccgcatgta ccagatccag 1380
tacaacagct cggctgatga catcctcgtc tacagggtgca gggtcaggc actggggtag 1440
```

<210> 19

<211> 1887

<212> DNA

<213> Homo sapiens

<400> 19

```
atggccatcc tcccgttget cctgtgcctg ctgccgctgg cccctgcctc atccccaccc 60
cagtcagcca caccagccc atgtcccgc cgctgccgt gccagacaca gtcgtgccc 120
ctaagcgtgc tgtgcccagg ggcaggcctc ctgttcgtgc caccctcgct ggaccgccgg 180
gcagccgagc tgcggctggc agacaacttc atcgctccg tgcgccgcg cgacctggcc 240
aacatgacag gcctgctgca tctgagcctg tcgcggaaca ccatccgcca cgtggctgcc 300
ggcgccctcg ccgacctgcg ggcctgcgt gccctgcacc tggatggcaa ccggtgacc 360
```

tcactggg	cagct	gcg	gtcaact	gccac	cctcag	420
aaccagct	cagcgct	ggccg	ctggatg	gtgccg	actggagg	480
ctcgacct	cctaca	cctcgag	ctgccc	aggcc	cgcctgg	540
aacgtca	cgttggg	cgaccaca	ctgctgg	ctgtgccc	cggcgctt	600
tcccgc	acaagct	cgggct	atgacct	accgc	cacaat	660
cccgac	tcttct	cctgccc	ctcgcc	cccggg	gcccgc	720
gccc	tggcctt	cggga	ctgcact	actgcg	ggtgtg	780
cgtcgc	cgcggg	cgacct	gcctgc	ccccac	tctggg	840
cgctact	ggg	cgaggag	tttgt	agccg	ggtgact	900
cgctac	ctctgg	gcccgc	cggccg	ccctgc	cgggcag	960
ggggac	agccc	gcgtt	tcacccc	gccc	aggca	1020
agcgtg	gcgcct	caatgg	ctggag	tggtc	gccggg	1080
ggtggc	tcacct	tgcggc	gcagct	aggcc	tgctgt	1140
ctgact	gtcccc	acctc	ctagcc	gcacc	tgacccc	1200
cgggac	atcctg	tctac	ccctc	cctctg	tgcca	1260
gcccga	ggccc	cgacc	gtccag	ctgag	ggccac	1320
gctctt	agtg	tcagc	atccc	tcgc	ccagat	1380
tacaac	cggctg	catac	tacagg	tccc	gagcc	1440
ttcctg	cggac	gtcag	acctac	tgtgc	cgccgt	1500
gaggac	ccacg	cacgg	cggc	gtgcg	cttctc	1560
gaacct	tgccg	cgggg	cacgc	tcctg	cacgat	1620
atcg	gcgc	cgtag	gtact	tcatt	gctgct	1680
cgctac	tgacg	ccagc	ggca	agatt	gcctgt	1740
agcgtt	cccag	cgggc	ggccc	ccacg	cccgc	1800
ccggag	cggcg	ggccc	gtggt	tggact	gcctg	1860
cccg	aacct	acctag				1887

<210> 20

<211> 2538

<212> DNA

<213> Homo sapiens

<400> 20

atgctgag	gcgtt	cctcag	ttaacc	ccggg	acagac	60
agtgc	ctgcc	catttg	atccg	tgtgc	aaagg	120
gtactga	tcaact	gaaca	tttaca	ttagc	ccagccc	180
cagtat	tctat	ttttc	ggaa	tgaca	gtatcca	240
gaattt	attact	cgcg	cttcac	gtaaca	gttac	300
atccga	gggcatt	tggc	actct	gactg	caaca	360
aagctt	tattg	ggacac	ctagg	agagc	gtatct	420
gccgact	attacat	tgccat	gctggg	tcagca	taaca	480
aaagt	tcctga	caacct	ctttc	ccagca	gttccg	540

```

gtcctgctga cccacttaga cctcaggggg aataggctaa aagtaatgcc ttttgcaggc 600
gtccttgaac atattggagg gatcatggag attcagctgg aggaaaatcc atggaattgc 660
acttgtgact tacttctctt caaggcctgg ctagacacca taactgtttt tgtgggagag 720
attgtctgtg agactccctt taggttgcac gggaaagacg tgaccagct gaccaggcaa 780
gacctctgtc ccagaaaaag tgccagtgat tccagtcaga ggggcagcca tgctgacacc 840
cacgtccaaa ggctgtcacc tacaatgaat cctgctctca acccaaccag ggctccgaaa 900
gccagccggc cgcccaaaat gagaaatcgt ccaactcctc gactgactgt gtcaaaggac 960
aggcaaagtt ttggacccat catggtgtac cagaccaagt ctctgtgcc tctcacctgt 1020
cccagcagct gtgtctgcac ctctcagagc tcagacaatg gtctgaatgt aaactgccaa 1080
gaaaggaagt tactaatat ctctgacctg cagcccaaac cgaccagtcc aaagaaactc 1140
tacctaacag ggaactatct tcaaactgtc tataagaatg acctcttaga atacagttct 1200
ttggacttac tgcacttagg aaacaacagg attgcagtca ttcaggaagg tgcctttaca 1260
aacctgacca gtttacgcag actttatctg aatggcaatt accttgaagt gctgtaccct 1320
tctatgtttg atggactgca gagcttgcaa tatctctatt tagagtataa tgcattaag 1380
gaaattaagc ctctgacctt tgatgctttg attaacctac agctactgtt tctgaacaac 1440
aaccttcttc ggtccttacc tgataatata tttgggggga cggccctaac caggctgaat 1500
ctgagaaaca accattttct tcacctgcc gtgaaagggg ttctggatca gctccggct 1560
ttcatccaga tagatctgca ggagaacccc tgggactgta cctgtgacat catggggctg 1620
aaagactgga cagaacatgc caattcccct gtcattatta atgaggtgac ttgcgaatct 1680
cctgctaagc atgcagggga gatactaaaa tttctgggga gggaggctat ctgtccagac 1740
agcccaact tgtcagatgg aacgtcttg tcaatgaatc acaatacaga cacacctcg 1800
tcgcttagtg tgtctcctag ttctatcct gaactacaca ctgaagttcc actgtctgtc 1860
ttaattctgg gattgcttgt tgttttcac ttatctgtct gttttggggc tggtttatc 1920
gtctttgtct tgaaacgccc aaagggagtg ccgagcgttc ccaggaatac caacaactta 1980
gacgtaagct cctttcaatt acagtatggg tcttacaaca ctgagactca cgataaaaca 2040
gacggccatg tctacaacta tatcccccca cctgtgggtc agatgtgcca aaaccccatc 2100
tacatgcaga aggaaggaga ccagtagcc tattaccgaa acctgcaaga gttcagctat 2160
agcaacctgg aggagaaaaa agaagagcca gccacacctg cttacacaat aagtgccact 2220
gagctgctag aaaagcaggc cacaccaaga gagcctgagc tgctgtatca aaatattgct 2280
gagcgagtca aggaacttcc cagcgcagc ctagtccact ataacttttg taccttacct 2340
aaaaggcagt ttgccccttc ctatgaatct cgacgcaaaa accaagacag aatcaataaa 2400
accgttttat atggaactcc caggaaatgc tttgtggggc agtcaaaacc caaccacct 2460
ttactgcaag ctaagccgca atcagaaccg gactacctcg aagttctgga aaaacaaact 2520
gcaatcagtc agctgtga 2538

```

<210> 21

<211> 1050

<212> DNA

<213> Homo sapiens

<400> 21

```

atggggatca cctgctggat cgccctgtat gctgtggagg ccctccccac ctgccctttc 60

```

```

tctctgcaagt gtgacagccg cagcctggag gtggactgca gtggccttgg cctcaccacg      120
gtgccccccag acgtgcccgc agccaccgga accctcttgc tcttgaacaa taagctgagt      180
gccctgccaa gctgggcttt cgccaacctc tccagcctgc agcggttgga cctgtccaac      240
aacttcctgg accggctgcc cgcctccatt ttcggggacc tgacgaatct gactgagctt      300
cagctgegca ataacagcat caggaccctg gacagggacc tgctgcggca ctgcgcgctg      360
ctccgccacc tggacctgtc catcaacggc ctggcccagt tgccccctgg tcttttcgac      420
gggctcctgg ctctgcgtc cctctcgctt cgctccaacc gtctgcagaa tctggaccgg      480
ctgacatttg aacccttagc aaactctgcag ctgctgcagg tcggggataa cccttgggag      540
tgtgactgta acctgcgtga gttcaaacac tggatggagt ggttctccta ccgaggggga      600
cgcttggacc agcttgcctg caccctgccc aaggagctga gggggaagga catgcggtg      660
gtcccatgag agatgttcaa ctactgctcc cagctggagg acgagaatag ctgagctggg      720
ctggatattc ctgggccacc ctgcaccaag gccagtccag agcctgctaa gccaagccc      780
ggggctgagc cggagccgga gccagcaca gcctgccac agaagcagag gcaccggccg      840
gcgagcgtga ggcgagccat gggcacggtg atcattgcag gggctcgtgtg cggcgctcgtc      900
tgcacatga tgggtggtggc cgctgcctat ggctgcatct acgcctccct catggccaag      960
taccaccggg agctcaaaaa gcgccagccc ctgatggggg accccgaggg cgagcacgag     1020
gaccagaagc agatctcttc tgtggcctga                                     1050

```

<210> 22

<211> 2215

<212> DNA

<213> Homo sapiens

<400> 22

```

atgggaatga ctgttataaa gcaaatacaca gatgacctat ttgtatggaa tgttctgaat      60
cgcaagaag taaacatcat ttgctgcgag aagggtggagc aggatgctgc tagagggatc     120
attcacatga ttttgaaaaa ggggttcagag tcctgtaacc tctttcttaa atcccttaag     180
gagtggaaact atcctctatt tcaggacttg aatggacaaa gtctttttca tcagacatca     240
gaaggagact tggacgattt ggctcaggat ttaaaggact tgtaccatac cccatctttt     300
ctgaactttt atccccttgg tgaagatatt gacattattt ttaacttgaa aagcaccttc     360
acagaacctg tcctgtggag gaaggaccaa caccatcacc gcgtggagca gctgacctg     420
aatggcctcc tgcaggctct tcagagcccc tgcattcttg aaggggaaatc tggcaaaggc     480
aagtccactc tgctgcagcg aattgccatg ctctggggct ccggaaagtg caaggctctg     540
accaagttca aattcgtctt ctctctccgt ctgagcaggg cccaggggtg actttttgaa     600
accctctgtg atcaactcct ggatatacct ggcacaaatca ggaagcagac attcatggcc     660
atgctgctga agctgcccga gagggttctt ttccttcttg atggctacaa tgaattcaag     720
cccagaact gccagaaaat cgaagccctg ataaaggaaa accaccgctt caagaacatg     780
gtcatcgtca ccactaccac tgagtgcctg aggcacatac ggcagtttgg tgccctgact     840
gctgaggttg gggatatgac agaagacagc gccagggctc tcatccgaga agtgcgtgac     900
aaggagcttg ctgaaggctt gttgctccaa attcagaaat ccaggtgctt gaggaatctc     960
atgaagacct ctctctttgt ggtcatcact tgtgcaatcc agatgggtga aagtgagttc     1020
cactctcaca cacaaacaac gctgttccat accttctatg atctgttgat acagaaaaac     1080

```

aaacacaaac	ataaaggtgt	ggctgcaagt	gacttcattc	ggagcctgga	ccactgtgga	1140
gacctagctc	tggagggtgt	gttctccac	aagtttgatt	tcgaactgca	ggatgtgtcc	1200
agcgtgaatg	aggatgtcct	gctgacaact	gggctcctct	gtaaatatac	agctcaaagg	1260
ttcaagccaa	agtataaatt	ctttcacaag	tcattccagg	agtacacagc	aggacgaaga	1320
ctcagcagtt	tattgacgtc	tcattgagcca	gaggaggtga	ccaaggggaa	tggttacttg	1380
cagaaaatgg	tttccatttc	ggacattaca	tccatttata	gcagcctgct	ccggtacacc	1440
tgtgggtcat	ctgtggaagc	caccagggct	gttatgaagc	acctcgcagc	agtgtatcaa	1500
cacggctgcc	ttctcggact	ttccatcgcc	aagaggcctc	tctggagaca	ggaatctttg	1560
caaagtgtga	aaaacaccac	tgagcaagaa	attctgaaag	ccataaacat	caattccttt	1620
gtagagtgtg	gcatccattt	atatcaagag	agtacatcca	aatcagccct	gagccaagaa	1680
tttgaagctt	tctttcaagg	taaaagctta	tatatcaact	cagggaacat	ccccgattac	1740
ttatttgact	tctttgaaca	tttgcccaat	tgtgcaagtg	ccctggactt	cattaaactg	1800
gacttttatg	ggggagctat	ggcttcattg	gaaaaggctg	cagaagacac	aggtggaatc	1860
cacatggaag	aggccccaga	aacctacatt	cccagcaggg	ctgtatcttt	gttcttcaac	1920
tggaagcagg	aattcaggac	tctggaggtc	acactccggg	atttcagcaa	gttgaataag	1980
caagatatca	gatatctggg	gaaaatatct	agctctgcca	caagcctcag	gctgcaataa	2040
aagagatgtg	ctgggtgtgg	tggaagcctc	agtttggtcc	tcagcacctg	taagaacatt	2100
tattctctca	tgggtggaag	cagtcacctc	accatagaag	atgagaggca	catcacatct	2160
gtaacaaacc	tgaaaacctt	gagtattcat	gacctacaga	atcaacggct	gccgg	2215

<210> 23

<211> 3213

<212> DNA

<213> Homo sapiens

<400> 23

atgtacaaaa	gccttaacat	tgacgagtgt	gatttgcattg	cctggctgga	tttgccctgcc	60
gagaaacctt	taggggtggt	taatcgggtc	tgctggggct	tcacaggtt	caaggggtac	120
atgtacccct	tggactactt	gaatttcata	aaggacaata	gccgagccct	tattcaaaga	180
atgggaatga	ctgttataaa	gcaaatcaca	gatgacctat	ttgtatggaa	tgttctgaat	240
cgcaagaag	taaacatcat	ttgctgcgag	aagggtggagc	aggatgctgc	tagagggatc	300
attcacatga	ttttgaaaaa	gggttcagag	tcctgtaacc	tctttcttaa	atcccttaag	360
gagtggaaact	atcctctatt	tcaggacttg	aatggacaaa	gtctttttca	tcagacatca	420
gaaggagact	tggacgattt	ggctcaggat	ttaaaggact	tgtaccatac	cccatctttt	480
ctgaactttt	atcccttgg	tgaagatatt	gacattattt	ttaacttgaa	aagcaccttc	540
acagaacctg	tcctgtggag	gaaggaccaa	caccatcacc	gcgtggagca	gctgacctg	600
aatggcctcc	tgcaggtctt	tcagagcccc	tgcattcttg	aagggggaatc	tggcaaaggc	660
aagtccactc	tgctgcagcg	aattgccatg	ctctggggct	ccggaaagtg	caaggctctg	720
accaagtcca	aattcgtctt	cttctctcgt	ctcagcaggg	cccaggggtg	actttttgaa	780
accctctgtg	atcaactcct	ggatatacct	ggcacaatca	ggaagcagac	attcatggcc	840
atgctgtgta	agctgcggca	gagggttctt	ttccttcttg	atggctacaa	tgaattcaag	900
ccccagaact	gccagaaat	cgaagccctg	ataaaggaaa	accaccgctt	caagaacatg	960


```

gtcatcgta ccactaccac tgagtgcctg aggcacatac ggaggtttgg tgccttgact 1020
gctgaggtgg gggatatgac agaagacagc gcccaggctc tcatccgaga agtgctgac 1080
aaggagcttg ctgaaggctt gttgctccaa attcagaaat ccaggtgctt gaggaatctc 1140
atgaagaccc ctctctttgt ggtcatcact tgtgcaatcc agatgggtga aagtgaagttc 1200
cactctcaca cacaacaac gctgttccat accttctatg atctgttgat acagaaaaac 1260
aaacacaaac ataaagggtg ggctgcaagt gacttcattc ggagcctgga ccactgtgga 1320
gacctagctc tggagggtgt gttctccac aagtttgatt tcgaactgca ggatgtgtcc 1380
agcgtgaatg aggatgtcct gctgacaact gggctcctct gtaaatatac agctcaaagg 1440
ttcaagccaa agtataaatt ctttcacaag tcattccagg agtacacagc aggacgaaga 1500
ctcagcagtt tattgacgtc tcatgagcca gaggaggtga ccaaggggaa tggttacttg 1560
cagaaaatgg tttccatttc ggacattaca tccacttata gcagcctgct ccggtacacc 1620
tgtgggtcat ctgtggaagc caccagggtc gttatgaagc acctcgcagc agtgatcaaa 1680
cacggctgcc ttctcggact ttccatcgcc aagaggcctc tctggagaca ggaatctttg 1740
caaagtgtga aaaacaccac tgagcaagaa attctgaaag ccataaacat caattccttt 1800
gtagagtgtg gcatccattt atatcaagag agtacatcca aatcagccct gagccaagaa 1860
tttgaagctt tctttcaagg taaaagctta tatatcaact cagggaaat ccccgattac 1920
ttatttgact tctttgaaca ttgccaat tgtgcaagt cctggactt cattaaactg 1980
gacttttatg ggggagctat ggcttcatgg gaaaaggctg cagaagacac aggtggaatc 2040
cacatggaag aggccccaga aacctacatt cccagcaggg ctgtatcttt gttcttcaac 2100
tggaagcagg aattcaggac tctggaggtc acactccggg atttcagcaa gttgaataag 2160
caagatatca gatattctgg gaaaatattc agctctgcca caagcctcag gctgcaaata 2220
aagagatgtg ctgggtgtgg tggaagcctc agtttggtcc tcagcacctg taagaacatt 2280
tattctctca tgggtgaagc cagtccctc accatagaag atgagaggca catcacatct 2340
gtaacaaacc tgaaaacctt gagtattcat gacctacaga atcaacggct gccgggtggt 2400
ctgactgaca gcttgggtaa cttgaagaac cttacaaagc tcataatgga taacataaag 2460
atgaatgaag aagatgctat aaaactagct gaaggcctga aaaacctgaa gaagatgtgt 2520
ttatttcatt tgaccactt gtctgacatt ggagagggaa tggattacat agtcaagtct 2580
ctgtcaagtg aacctgtga ccttgaagaa attcaattag tctcctgctg cttgtctgca 2640
aatgcagtga aaatcctagc tcagaatctt cacaatttgg tcaaactgag cattcttgat 2700
ttatcagaaa attacctgga aaaagatgga aatgaagctc ttcattgaact gatcgacagg 2760
atgaacgtgc tagaacagct caccgcactg atgctgccct ggggctgtga cgtgcaaggc 2820
agcctgagca gcctgttgaa acatttgag gaggtccac aactcgtaa gcttgggttg 2880
aaaaactgga gactcacaga tacagagatt agaatttttag gtgcattttt tggaaagaac 2940
cctctgaaaa acttccagca gttgaatttg ggggaaatc gtgtgagcag tgatggatgg 3000
cttgccctta tgggtgtatt tgagaatctt aagcaattag tgttttttga ctttagtact 3060
aaagaatttc tacctgatcc agcattagtc agaaaactta gccaaagtgt atccaagtta 3120
acttttctgc aagaagctag gcttgttggg tggcaatttg atgatgatga tctcagtggt 3180
attacagggtg cttttaaaact agtaactgct taa 3213

```

<210> 24

<211> 1464

<212> DNA

<213> Homo sapiens

<400> 24

```

atgccgcctt tggcacagt gtccttttct cgtccagacc actgccatgt gactttcgtg      60
accctcaagt gtgactcctc caagaagagg cgccgtggcc gcaagtcccc atccaaggag     120
gtgtcccaca tcacagcaga gtttgagatc gagacaaaga tgggaagggc ctcagacaca     180
tgcgaagcgg actgcttgcg gaagcgagca gaacagagcc tgcaggccgc catcaagacc     240
ctgcgcaagt ccatcgcccg gcagcagttc tatgtccagg tctcaggcac tgagtacgag     300
gtagcccaga ggccagccaa ggcgctggag gggcaggggg catgtggcgc aggccagggtg     360
ctacaggaca gcaaatgctg tgctgtggg cctggcacc cttcgggtgg tgagctcggc     420
cagtgtgtgt catgtatgcc aggaacatac caggacatgg aaggccagct cagttgcaca     480
ccgtgcccga gcagcgacgg gcttggtctg cctgggtgcc gcaacgtgtc ggaatgtgga     540
ggcaagtgcg ggcctagaag gagaggcttc ttctcgcccg atggcttcaa gccctgccag     600
gcctgccccg tgggcacgta ccagcctgag cccggggcga ccggctgctt ccctgtgga     660
gggggtttgc tcaccaaaca cgaaggcacc acctccttcc aggactgcga ggctaaagtg     720
cactgctccc ccggccacca ctacaacacc accacccacc gctgcatccg ctgccccgtc     780
ggcacctacc agcccaggtt tggccagaac cactgcatca cctgtccggg caacaccagc     840
acagacttcg atggctccac caacgtcaca cactgcaaaa accagcactg cggcggcgag     900
cttggtgact acaccggcta catcgagtcc cccaactacc ctggcgacta ccagccaac     960
gctgaatgcg tctggcacat cgcgcctccc ccaaagcgca ggatcctcat cgtggctcct     1020
gagatcttcc tgcccatcga ggatgagtgc ggcgatgttc tggcatgag gaagagtgcc     1080
tctccacagt ccatcaccac ctatgagacc tgccagacct acgagaggcc catcgcttc     1140
acctcccgt cccgcaagct ctggatccag ttcaaatacca atgaaggcaa cagcggcaaa     1200
ggcttccaag tgccctatgt cacctacgat gaggactacc agcaactcat agaggacatc     1260
gtgcgcgatg ggcgctgta cgctcggag aaccaccagg aaattttgaa agacaagaag     1320
ctgatcaagg ccctcttcga cgtgctggcg catccccaga actacttcaa gtacacagcc     1380
caggaatcca aggagatgtt cccacgggtc ttcataaac tgctgcgctc caaagtgtct     1440
cggttcctgc ggccctacaa ataa                                           1464

```

<210> 25

<211> 2897

<212> DNA

<213> Homo sapiens

<400> 25

```

atgggcgcgg cggccgtgcg ctggcacttg tgcgtgctgc tggccctggg cacacgcggg      60
cggctggccg ggggcagcgg gctcccaggt tcagtcgacg tggatgagtg ctcagagggc     120
acagatgact gccacatcga tgccatctgt cagaacacgc ccaagtccta caaatgcctc     180
tgcaagccag gctacaaggg ggaaggcaag cagtgtgaag acattgacga gtgtgagaat     240
gactactaca atgggggctg tgtccacgag tgcataaca tcccggggaa ctacagggtg     300
acctgctttg atggcttcat gctggcacac gatggacaca actgcctgga tgtggacgag     360
tgtcaggaca ataatggtgg ctgccagcag atctgcgtca atgcatggg cagctacgag     420

```

tgtagtgcc	acagtggctt	cttccttagt	gacaaccagc	atacctgcat	ccaccgctcc	480
aatgagggta	tgaactgcat	gaacaaagac	catggctgtg	cccacatctg	ccgggagacg	540
cccaaaggtg	gggtggcctg	cgactgcagg	cccggctttg	accttgccca	aaaccagaag	600
gactgcacac	taacctgtaa	ttatggaaac	ggaggctgcc	agcacagctg	tgaggacaca	660
gacacaggcc	ccacgtgtgg	ttgccaccag	aagtacgccc	tccactcaga	cggtcgcacg	720
tgcatcgaga	cgtgcgcagt	caataacgga	ggctgcgacc	ggacatgcaa	ggacacagcc	780
actggcgctg	gatgcagctg	ccccgttga	ttcacactgc	agccggacgg	gaagacatgc	840
aaagacatca	acgagtgcct	ggtcaacaac	ggaggctgcg	accacttctg	ccgcaacacc	900
gtgggcagct	tcgagtgcgg	ctgccggaag	ggctacaagc	tgctcaccga	cgagcgcacc	960
tgccaggaca	tcgacgagtg	ctccttcgag	cggacctgtg	accacatctg	catcaactcc	1020
ccgggcagct	tccagtgcct	gtgtcaccgc	ggctacatcc	tctacgggac	aacccactgc	1080
ggagatgtgg	acgagtgcag	catgagcaac	gggagctgtg	accagggctg	cgtcaacacc	1140
aagggcagct	acgagtgcgt	ctgtcccccg	gggaggcggc	tccactggaa	cgggaaggat	1200
tgcgtaggaga	caggcaagtg	tctttctcgc	gccaagacct	ccccccgggc	ccagctgtcc	1260
tgacgcaagg	caggcgggtg	ggagagctgc	ttcctttcct	gcccggctca	cacactcttc	1320
gtgccagact	cggaaaatag	ctacgtcctg	agctgcggag	ttccaggggc	gcagggcaag	1380
gcgctgcaga	aacgcaacgg	caccagctct	ggcctcgggc	ccagctgctc	agatgcccc	1440
accaccccc	tcaaacagaa	ggcccgttc	aagatccgag	atgccaaagt	ccacctccgg	1500
ccccacagcc	aggcacgagc	aaaggagacc	gccaggcagc	cgctgctgga	ccactgccat	1560
gtgactttcg	tgacctcaa	gtgtgactcc	tccaagaaga	ggcgccgtgg	ccgcaagtcc	1620
ccatccaagg	aggtgtccca	catcacagca	gagtttgaga	tcgagacaaa	gatggaagag	1680
gcctcagaca	catgcgaagc	ggactgcttg	cggaagcgag	cagaacagag	cctgcaggcc	1740
gccatcaaga	ccctgcgcaa	gtccatcggc	cggcagcagt	tctatgtcca	ggtctcaggc	1800
actgagtacg	aggtagccca	gaggccagcc	aaggcgctgg	aggggcaggg	ggcatgtggc	1860
gcaggccagg	tgctacagga	cagcaaatgc	gttgccctgtg	ggcctggcac	ccacttcggt	1920
ggtgagctcg	gccagtgtgt	gtcatgtatg	ccagggaacat	accaggacat	ggaaggccag	1980
ctcagttgca	caccgtgccc	cagcagcgac	gggcttggtc	tgcttggtgc	ccgcaacgtg	2040
tcggaatgtg	gaggccagtg	ttctccaggc	ttcttctcgg	ccgatggctt	caagccctgc	2100
caggcctgcc	ccgtgggcac	gtaccagcct	gagcccgggc	gcaccggctg	cttccccctgt	2160
ggaggggggt	tgctcaccaa	acacgaaggc	accacctcct	tccaggactg	cgaggctaaa	2220
gtgcactgct	ccccgggcca	ccactacaac	accaccacc	accgctgcat	ccgtgcccc	2280
gtcggcacct	accagccoga	gtttggccag	aaccactgca	tcacctgtcc	gggcaacacc	2340
agcacagact	tcgatggctc	caccaacgtc	acacactgca	aaaaccagca	ctgcggcggc	2400
gagcttggtg	actacacggg	ctacatcgag	tccccaaact	accctggcga	ctaccagacc	2460
aacgctgaat	gcgtctggca	catcgcgctt	cccccaaagc	gcaggatcct	catcgtggtc	2520
cctgagatct	tcctgcccc	cgaggatgag	tgcggcgatg	ttctggatcat	gaggaagagt	2580
gcctctccca	cgtccatcac	cacctatgag	acctgccaga	cctacgagag	gcccatcgcc	2640
ttcacctccc	gtccccgcaa	gctctggatc	cagttcaa	ccaatgaagg	caacagcggc	2700
aaaggcttcc	aagtgcctta	tgctacctac	gatggtaaga	tccactgtct	tcacggccca	2760
ctgtgcacgg	ctcaggcggg	gccctggaga	cacagagatg	agtgcacgt	ccccgcccc	2820
tcaggagct	gcgacctggc	aggtacagac	ctggaagcag	aacgaacact	gtcagggggc	2880
agagccagac	aggctga					2897

<210> 26
 <211> 2151
 <212> DNA
 <213> Homo sapiens

<400> 26

```

atggctagga tgagctttgt tatagcagct tgccaattgg tgctgggcct actaatgact      60
tcattaaccg agtcttccat acagaatagt gagtgtccac aactttgcgt atgtgaaatt      120
cgtccctggg ttaccccaca gtcaacttac agagaagcca ccactgttga ttgcaatgac      180
ctccgcttaa caaggattcc cagtaacctc tctagtga caacaagtgt tctcttacag      240
agcaataaca tcgcaaagac tgtggatgag ctgcagcagc ttttcaactt gactgaacta      300
gatttctccc aaaacaactt tactaacatt aaggaggctg ggctggcaaa cctaaccag      360
ctcacaacgc tgcatttggg ggaaaatcag attaccgaga tgactgatta ctgtctacaa      420
gacctcagca accttcaaga actctacatc aaccacaacc aaattagcac tatttctgct      480
catgcttttg caggcttaaa aaatctatta aggctccacc tgaactcaa caaattgaaa      540
gttattgata gtcgctggtt tgattctaca cccaacctgg aaattctcat gatcggagaa      600
aaccctgtga ttggaattct ggatatgaac ttcaaacccc tcgcaaattt gagaagctta      660
gttttggcag gaatgtatct cactgatatt cctggaaatg ctttgggtggg tctggatagc      720
cttgagagcc tgtcttttta tgataacaaa ctgggttaaag tccctcaact tgccctgcaa      780
aaagttccaa atttgaaatt cttagacctc aacaaaaacc ccattcacaa aatccaagaa      840
ggggacttca aaaatatgct tcggttaaaa gaactgggaa tcaacaatat gggcgagctc      900
gtttctgtcg accgctatgc cctggataac ttgcctgaac tcacaaaagct ggaagccacc      960
aataacccta aactctctta catccaccgc ttggctttcc gaagtgtccc tgctctggaa     1020
agcttgatgc tgaacaacaa tgccttgaat gccatttacc aaaagacagt cgaatccctc     1080
cccaatctgc gtgagatcag tatccatagc aatcccctca ggtgtgactg tgtgatccac     1140
tggaattaact ccaacaaaac caacatccgc ttcattggagc ccctgtccat gttctgtgcc     1200
atgccgcccg aatataaagg gcaccagggtg aaggaagttt taatccagga ttcgagtga     1260
cagtgcctcc caatgatatc tcacgacagc ttcccaaadc gtttaaactg ggatatcggc     1320
acgacgggtt tcttagactg tcgagccatg gctgagccag aacctgaaat ttactgggtc     1380
actcccattg gaaataagat aactgtggaa accctttcag ataaatacaa gctaagtagc     1440
gaaggtacct tggaaatata taacatacaa attgaagact caggaagata cacatgtgtt     1500
gcccagaatg tccaaggggc agacactcgg gtggcaacaa ttaaggttta tgggaccctt     1560
ctggatggta ccaggtgct aaaaatatac gtcaagcaga cagaatccca ttccatctta     1620
gtgtcctgga aagttaattc caatgtcatg acgtcaaact taaaatgggtc gtctgccacc     1680
atgaagattg ataaccctca cataacatat actgccaggg tcccagtcga tgtccatgaa     1740
tacaacctaa cgcattctga gccttcaca gattatgaag tgtgtctcac agtgtccaat     1800
attcatcagc agactcaaaa gtcatgcgta aatgtcacaa ccaaaaatgc cgccttcgca     1860
gtggacatct ctgatcaaga aaccagtaca gcccttgctg cagtaatggg gtctatgttt     1920
gccgtcatta gccttcgctc cattgtctgt tactttgcc aagattttaa gagaaaaaac     1980
taccaccact cattaaaaaa gtatatgcaa aaaacctctt caatccact aaatgagctg     2040
taccaccac tcattaacct ctgggaaggt gacagcgaga aagacaaaga tggttctgca     2100

```

gacaccaagc caacccaggt cgacacatcc agaagctatt acatgtggtta a

2151

<210> 27

<211> 766

<212> PRT

<213> Homo sapiens

<400> 27

Met	Glu	Lys	Val	Leu	Phe	Tyr	Leu	Phe	Leu	Ile	Gly	Ile	Ala	Val	Lys
1				5					10					15	
Ala	Gln	Ile	Cys	Pro	Lys	Arg	Cys	Val	Cys	Gln	Ile	Leu	Ser	Pro	Asn
			20					25					30		
Leu	Ala	Thr	Leu	Cys	Ala	Lys	Lys	Gly	Leu	Leu	Phe	Val	Pro	Pro	Asn
		35					40					45			
Ile	Asp	Arg	Arg	Thr	Val	Glu	Leu	Arg	Leu	Ala	Asp	Asn	Phe	Val	Thr
	50					55					60				
Asn	Ile	Lys	Arg	Lys	Asp	Phe	Ala	Asn	Met	Thr	Ser	Leu	Val	Asp	Leu
65				70					75					80	
Thr	Leu	Ser	Arg	Asn	Thr	Ile	Ser	Phe	Ile	Thr	Pro	His	Ala	Phe	Ala
				85				90						95	
Asp	Leu	Arg	Asn	Leu	Arg	Ala	Leu	His	Leu	Asn	Ser	Asn	Arg	Leu	Thr
			100					105					110		
Lys	Ile	Thr	Asn	Asp	Met	Phe	Ser	Gly	Leu	Ser	Asn	Leu	His	His	Leu
	115					120					125				
Ile	Leu	Asn	Asn	Asn	Gln	Leu	Thr	Leu	Ile	Ser	Ser	Thr	Ala	Phe	Asp
	130					135					140				
Asp	Val	Phe	Ala	Leu	Glu	Glu	Leu	Asp	Leu	Ser	Tyr	Asn	Asn	Leu	Glu
145				150					155					160	
Thr	Ile	Pro	Trp	Asp	Ala	Val	Glu	Lys	Met	Val	Ser	Leu	His	Thr	Leu
				165				170						175	
Ser	Leu	Asp	His	Asn	Met	Ile	Asp	Asn	Ile	Pro	Lys	Gly	Thr	Phe	Ser
			180					185					190		
His	Leu	His	Lys	Met	Thr	Arg	Leu	Asp	Val	Thr	Ser	Asn	Lys	Leu	Gln
	195					200					205				
Lys	Leu	Pro	Pro	Asp	Pro	Leu	Phe	Gln	Arg	Ala	Gln	Val	Leu	Ala	Thr
	210					215					220				
Ser	Gly	Ile	Ile	Ser	Pro	Ser	Thr	Phe	Ala	Leu	Ser	Phe	Gly	Gly	Asn
225				230					235					240	
Pro	Leu	His	Cys	Asn	Cys	Glu	Leu	Leu	Trp	Leu	Arg	Arg	Leu	Ser	Arg
			245					250					255		
Glu	Asp	Asp	Leu	Glu	Thr	Cys	Ala	Ser	Pro	Pro	Leu	Leu	Thr	Gly	Arg
	260					265					270				

22/66

Tyr Phe Trp Ser Ile Pro Glu Glu Glu Phe Leu Cys Glu Pro Pro Leu
 275 280 285
 Ile Thr Arg His Thr His Glu Met Arg Val Leu Glu Gly Gln Arg Ala
 290 295 300
 Thr Leu Arg Cys Lys Ala Arg Gly Asp Pro Glu Pro Ala Ile His Trp
 305 310 315 320
 Ile Ser Pro Glu Gly Lys Leu Ile Ser Asn Ala Thr Arg Ser Leu Val
 325 330 335
 Tyr Asp Asn Gly Thr Leu Asp Ile Leu Ile Thr Thr Val Lys Asp Thr
 340 345 350
 Gly Ala Phe Thr Cys Ile Ala Ser Asn Pro Ala Gly Glu Ala Thr Gln
 355 360 365
 Ile Val Asp Leu His Ile Ile Lys Leu Pro His Leu Leu Asn Ser Thr
 370 375 380
 Asn His Ile His Glu Pro Asp Pro Gly Ser Ser Asp Ile Ser Thr Ser
 385 390 395 400
 Thr Lys Ser Gly Ser Asn Thr Ser Ser Ser Asn Gly Asp Thr Lys Leu
 405 410 415
 Ser Gln Asp Lys Ile Val Val Ala Glu Ala Thr Ser Ser Thr Ala Leu
 420 425 430
 Leu Lys Phe Asn Phe Gln Arg Asn Ile Pro Gly Ile Arg Met Phe Gln
 435 440 445
 Ile Gln Tyr Asn Gly Thr Tyr Asp Asp Thr Leu Val Tyr Arg Met Ile
 450 455 460
 Pro Pro Thr Ser Lys Thr Phe Leu Val Asn Asn Leu Ala Ala Gly Thr
 465 470 475 480
 Met Tyr Asp Leu Cys Val Leu Ala Ile Tyr Asp Asp Gly Ile Thr Ser
 485 490 495
 Leu Thr Ala Thr Arg Val Val Gly Cys Ile Gln Phe Thr Thr Glu Gln
 500 505 510
 Asp Tyr Val Arg Cys His Phe Met Gln Ser Gln Phe Leu Gly Gly Thr
 515 520 525
 Met Ile Ile Ile Ile Gly Gly Ile Ile Val Ala Ser Val Leu Val Phe
 530 535 540
 Ile Ile Ile Leu Met Ile Arg Tyr Lys Val Cys Asn Asn Asn Gly Gln
 545 550 555 560
 His Lys Val Thr Lys Val Ser Asn Val Tyr Ser Gln Thr Asn Gly Ala
 565 570 575
 Gln Ile Gln Gly Cys Ser Val Thr Leu Pro Gln Ser Val Ser Lys Gln
 580 585 590
 Ala Val Gly His Glu Glu Asn Ala Gln Cys Cys Lys Ala Thr Ser Asp
 595 600 605

Asn Val Ile Gln Ser Ser Glu Thr Cys Ser Ser Gln Asp Ser Ser Thr
 610 615 620
 Thr Thr Ser Ala Leu Pro Pro Ser Trp Thr Ser Ser Thr Ser Val Ser
 625 630 635 640
 Gln Lys Gln Lys Arg Lys Thr Gly Thr Lys Pro Ser Thr Glu Pro Gln
 645 650 655
 Asn Glu Ala Val Thr Asn Val Glu Ser Gln Asn Thr Asn Arg Asn Asn
 660 665 670
 Ser Thr Ala Leu Gln Leu Ala Ser Arg Pro Pro Asp Ser Val Thr Glu
 675 680 685
 Gly Pro Thr Ser Lys Arg Ala His Ile Lys Pro Ser Lys Phe Ile Thr
 690 695 700
 Leu Pro Ala Glu Arg Ser Gly Ala Arg His Lys Tyr Ser Leu Asn Gly
 705 710 715 720
 Glu Leu Lys Glu Tyr Tyr Cys Tyr Ile Asn Ser Pro Asn Thr Cys Gly
 725 730 735
 Leu Phe Pro Lys Arg Ser Met Ser Met Asn Val Met Phe Ile Gln Ser
 740 745 750
 Asp Cys Ser Asp Gly His Ser Gly Lys Ala Thr Leu Lys Phe
 755 760 765

<210> 28

<211> 148

<212> PRT

<213> Homo sapiens

<400> 28

Ala Met Leu Gly Leu Pro Trp Lys Gly Gly Leu Ser Trp Ala Leu Leu
 1 5 10 15
 Leu Leu Leu Leu Gly Ser Gln Ile Leu Leu Ile Tyr Ala Trp His Phe
 20 25 30
 His Glu Gln Arg Asp Cys Asp Glu His Asn Val Met Ala Arg Tyr Leu
 35 40 45
 Pro Ala Thr Val Glu Phe Ala Val His Thr Phe Asn Gln Gln Ser Lys
 50 55 60
 Asp Tyr Tyr Ala Tyr Arg Leu Gly His Ile Leu Asn Ser Trp Lys Glu
 65 70 75 80
 Gln Val Glu Ser Lys Thr Val Phe Ser Met Glu Leu Leu Leu Gly Arg
 85 90 95
 Thr Arg Cys Gly Lys Phe Glu Asp Asp Ile Asp Asn Cys His Phe Gln
 100 105 110
 Glu Ser Thr Glu Leu Asn Asn Thr Phe Thr Cys Phe Phe Thr Ile Ser

115 120 125
 Thr Arg Pro Trp Met Thr Gln Phe Ser Leu Leu Asn Lys Thr Cys Leu
 130 135 140
 Glu Gly Phe His
 145

<210> 29
 <211> 159
 <212> PRT
 <213> Homo sapiens

<400> 29
 Asx Met Trp Ser Leu Pro Pro Ser Arg Ala Leu Ser Cys Ala Pro Leu
 1 5 10 15
 Leu Leu Leu Phe Ser Phe Gln Phe Leu Val Thr Tyr Ala Trp Arg Phe
 20 25 30
 Gln Glu Glu Glu Glu Trp Asn Asp Gln Lys Gln Ile Ala Val Tyr Leu
 35 40 45
 Pro Pro Thr Leu Glu Phe Ala Val Tyr Thr Phe Asn Lys Gln Ser Lys
 50 55 60
 Asp Trp Tyr Ala Tyr Lys Leu Val Pro Val Leu Ala Ser Trp Lys Glu
 65 70 75 80
 Gln Gly Tyr Asp Lys Met Thr Phe Ser Met Asn Leu Gln Leu Gly Arg
 85 90 95
 Thr Met Cys Gly Lys Phe Glu Asp Asp Ile Asp Asn Cys Pro Phe Gln
 100 105 110
 Glu Ser Pro Glu Leu Asn Asn Val Arg Gln Asp Thr Ser Phe Pro Pro
 115 120 125
 Gly Tyr Ser Cys Gly Cys Arg Met Gly Cys Gly Ala Asp Thr Asp Leu
 130 135 140
 His Leu Leu Leu His His Trp Asn Arg Ala Leu Glu Asp Thr Val
 145 150 155

<210> 30
 <211> 148
 <212> PRT
 <213> Homo sapiens

<400> 30
 Asx Met Trp Ser Leu Pro Pro Ser Arg Ala Leu Ser Cys Ala Pro Leu
 1 5 10 15
 Leu Leu Leu Phe Ser Phe Gln Phe Leu Val Thr Tyr Ala Trp Arg Phe

20 25 30
 Gln Glu Glu Glu Glu Trp Asn Asp Gln Lys Gln Ile Ala Val Tyr Leu
 35 40 45
 Pro Pro Thr Leu Glu Phe Ala Val Tyr Thr Phe Asn Lys Gln Ser Lys
 50 55 60
 Asp Trp Tyr Ala Tyr Lys Leu Val Pro Val Leu Ala Ser Trp Lys Glu
 65 70 75 80
 Gln Gly Tyr Asp Lys Met Thr Phe Ser Met Asn Leu Gln Leu Gly Arg
 85 90 95
 Thr Met Cys Gly Lys Phe Glu Asp Asp Ile Asp Asn Cys Pro Phe Gln
 100 105 110
 Glu Ser Pro Glu Leu Asn Asn Thr Cys Thr Cys Phe Phe Thr Ile Gly
 115 120 125
 Ile Glu Pro Trp Arg Thr Arg Phe Asp Leu Trp Asn Lys Thr Cys Ser
 130 135 140
 Gly Gly His Ser
 145

<210> 31
 <211> 820
 <212> PRT
 <213> Homo sapiens

<400> 31
 Met Leu Arg Leu Gly Leu Cys Ala Ala Ala Leu Leu Cys Val Cys Arg
 1 5 10 15
 Pro Gly Ala Val Arg Ala Asp Cys Trp Leu Ile Glu Gly Asp Lys Gly
 20 25 30
 Tyr Val Trp Leu Ala Ile Cys Ser Gln Asn Gln Pro Pro Tyr Glu Thr
 35 40 45
 Ile Pro Gln His Ile Asn Ser Thr Val His Asp Leu Arg Leu Asn Glu
 50 55 60
 Asn Lys Leu Lys Ala Val Leu Tyr Ser Ser Leu Asn Arg Phe Gly Asn
 65 70 75 80
 Leu Thr Asp Leu Asn Leu Thr Lys Asn Glu Ile Ser Tyr Ile Glu Asp
 85 90 95
 Gly Ala Phe Leu Gly Gln Ser Ser Leu Gln Val Leu Gln Leu Gly Tyr
 100 105 110
 Asn Lys Leu Ser Asn Leu Thr Glu Gly Met Leu Arg Gly Met Ser Arg
 115 120 125
 Leu Gln Phe Leu Phe Val Gln His Asn Leu Ile Glu Val Val Thr Pro
 130 135 140

Thr Ala Phe Ser Glu Cys Pro Ser Leu Ile Ser Ile Asp Leu Ser Ser
 145 150 155 160
 Asn Arg Leu Ser Arg Leu Asp Gly Ala Thr Phe Ala Ser Leu Ala Ser
 165 170 175
 Leu Met Val Cys Glu Leu Ala Gly Asn Pro Phe Asn Cys Glu Cys Asp
 180 185 190
 Leu Phe Gly Phe Leu Ala Trp Leu Val Val Phe Asn Asn Val Thr Lys
 195 200 205
 Asn Tyr Asp Arg Leu Gln Cys Glu Ser Pro Arg Glu Phe Ala Gly Tyr
 210 215 220
 Pro Leu Leu Val Pro Arg Pro Tyr His Ser Leu Asn Ala Ile Thr Val
 225 230 235 240
 Leu Gln Ala Lys Cys Arg Asn Gly Ser Leu Pro Ala Arg Pro Val Ser
 245 250 255
 His Pro Thr Pro Tyr Ser Thr Asp Ala Gln Arg Glu Pro Asp Glu Asn
 260 265 270
 Ser Gly Phe Asn Pro Asp Glu Ile Leu Ser Val Glu Pro Pro Ala Ser
 275 280 285
 Ser Thr Thr Asp Ala Ser Ala Gly Pro Ala Ile Lys Leu His His Val
 290 295 300
 Thr Phe Thr Ser Ala Thr Leu Val Val Ile Ile Pro His Pro Tyr Ser
 305 310 315 320
 Lys Met Tyr Ile Leu Val Gln Tyr Asn Asn Ser Tyr Phe Ser Asp Val
 325 330 335
 Met Thr Leu Lys Asn Lys Lys Glu Ile Val Thr Leu Asp Lys Leu Arg
 340 345 350
 Ala His Thr Glu Tyr Thr Phe Cys Val Thr Ser Leu Arg Asn Ser Arg
 355 360 365
 Arg Phe Asn His Thr Cys Leu Thr Phe Thr Thr Arg Asp Pro Val Pro
 370 375 380
 Gly Asp Leu Ala Pro Ser Thr Ser Thr Thr Thr His Tyr Ile Met Thr
 385 390 395 400
 Ile Leu Gly Cys Leu Phe Gly Met Val Ile Val Leu Gly Ala Val Tyr
 405 410 415
 Tyr Cys Leu Arg Lys Arg Arg Met Gln Glu Glu Lys Gln Lys Ser Val
 420 425 430
 Asn Val Lys Lys Thr Ile Leu Glu Met Arg Tyr Gly Ala Asp Val Asp
 435 440 445
 Ala Gly Ser Ile Val His Ala Ala Gln Lys Leu Gly Glu Pro Pro Val
 450 455 460
 Leu Pro Val Ser Arg Met Ala Ser Ile Pro Ser Met Ile Gly Glu Lys
 465 470 475 480

WO 01/66690

Leu Pro Thr Ala Lys Gly Leu Glu Ala Gly Leu Asp Thr Pro Lys Val
 485 490 495
 Ala Thr Lys Gly Asn Tyr Ile Glu Val Arg Thr Gly Ala Gly Gly Asp
 500 505 510
 Gly Leu Ala Arg Pro Glu Asp Asp Leu Pro Asp Leu Glu Asn Gly Gln
 515 520 525
 Gly Ser Ala Ala Glu Ile Ser Thr Ile Ala Lys Glu Val Asp Lys Val
 530 535 540
 Asn Gln Ile Ile Asn Asn Cys Ile Asp Ala Leu Lys Leu Asp Ser Ala
 545 550 555 560
 Ser Phe Leu Gly Gly Gly Ser Ser Ser Gly Asp Pro Glu Leu Ala Phe
 565 570 575
 Glu Cys Gln Ser Leu Pro Ala Ala Ala Ala Ser Ser Ala Thr Gly
 580 585 590
 Pro Gly Ala Leu Glu Arg Pro Ser Phe Leu Ser Pro Pro Tyr Lys Glu
 595 600 605
 Ser Ser His His Pro Leu Gln Arg Gln Leu Ser Ala Asp Ala Ala Val
 610 615 620
 Thr Arg Lys Thr Cys Ser Val Ser Ser Ser Gly Ser Ile Lys Ser Ala
 625 630 635 640
 Lys Val Phe Ser Leu Asp Val Pro Asp His Pro Ala Ala Thr Gly Leu
 645 650 655
 Ala Lys Gly Asp Ser Lys Tyr Ile Glu Lys Gly Ser Pro Leu Asn Ser
 660 665 670
 Pro Leu Asp Arg Leu Pro Leu Val Pro Ala Gly Ser Gly Gly Gly Ser
 675 680 685
 Gly Gly Gly Gly Gly Ile His His Leu Glu Val Lys Pro Ala Tyr His
 690 695 700
 Cys Ser Glu His Arg His Ser Phe Pro Ala Leu Tyr Tyr Glu Glu Gly
 705 710 715 720
 Ala Asp Ser Leu Ser Gln Arg Val Ser Phe Leu Lys Pro Leu Thr Arg
 725 730 735
 Ser Lys Arg Asp Ser Thr Tyr Ser Gln Leu Ser Pro Arg His Tyr Tyr
 740 745 750
 Ser Gly Tyr Ser Ser Ser Pro Glu Tyr Ser Ser Glu Ser Thr His Lys
 755 760 765
 Ile Trp Glu Arg Phe Arg Pro Tyr Lys Lys His His Arg Glu Glu Val
 770 775 780
 Tyr Met Ala Ala Gly His Ala Leu Arg Lys Lys Val Gln Phe Ala Lys
 785 790 795 800
 Asp Glu Asp Leu His Asp Ile Leu Asp Tyr Trp Lys Gly Val Ser Ala
 805 810 815

Gln Gln Lys Leu
820

<210> 32

<211> 866

<212> PRT

<213> Homo sapiens

<400> 32

```

Met Thr Ile Glu Lys Met Phe Ser Phe Tyr Phe Leu Asp Tyr Phe Ser
 1           5           10           15
Leu Phe Arg Ser Ile Gln Leu Phe Ala Asp Cys Lys Lys Met Phe Leu
 20           25           30
Trp Leu Phe Leu Ile Leu Ser Ala Leu Ile Ser Ser Thr Asn Ala Asp
 35           40           45
Ser Asp Ile Ser Val Glu Ile Cys Asn Val Cys Ser Cys Val Ser Val
 50           55           60
Glu Asn Val Leu Tyr Val Asn Cys Glu Lys Val Ser Val Tyr Arg Pro
 65           70           75           80
Asn Gln Leu Lys Pro Pro Trp Ser Asn Phe Tyr His Leu Asn Phe Gln
 85           90           95
Asn Asn Phe Leu Asn Ile Leu Tyr Pro Asn Thr Phe Leu Asn Phe Ser
100          105          110
His Ala Val Ser Leu His Leu Gly Asn Asn Lys Leu Gln Asn Ile Glu
115          120          125
Gly Gly Ala Phe Leu Gly Leu Ser Ala Leu Lys Gln Leu His Leu Asn
130          135          140
Asn Asn Glu Leu Lys Ile Leu Arg Ala Asp Thr Phe Leu Gly Ile Glu
145          150          155          160
Asn Leu Glu Tyr Leu Gln Ala Asp Tyr Asn Leu Ile Lys Tyr Ile Glu
165          170          175
Arg Gly Ala Phe Asn Lys Leu His Lys Leu Lys Val Leu Ile Leu Asn
180          185          190
Asp Asn Leu Ile Ser Phe Leu Pro Asp Asn Ile Phe Arg Phe Ala Ser
195          200          205
Leu Thr His Leu Asp Ile Arg Gly Asn Arg Ile Gln Lys Leu Pro Tyr
210          215          220
Ile Gly Val Leu Glu His Ile Gly Arg Val Val Glu Leu Gln Leu Glu
225          230          235          240
Asp Asn Pro Trp Asn Cys Ser Cys Asp Leu Leu Pro Leu Lys Ala Trp
245          250          255
Leu Glu Asn Met Pro Tyr Asn Ile Tyr Ile Gly Glu Ala Ile Cys Glu

```

260	265	270
Thr Pro Ser Asp Leu Tyr Gly Arg Leu Leu Lys Glu Thr Asn Lys Gln		
275	280	285
Glu Leu Cys Pro Met Gly Thr Gly Ser Asp Phe Asp Val Arg Ile Leu		
290	295	300
Pro Pro Ser Gln Leu Glu Asn Gly Tyr Thr Thr Pro Asn Gly His Thr		
305	310	315
Thr Gln Thr Ser Leu His Arg Leu Val Thr Lys Pro Pro Lys Thr Thr		
325	330	335
Asn Pro Ser Lys Ile Ser Gly Ile Val Ala Gly Lys Ala Leu Ser Asn		
340	345	350
Arg Asn Leu Ser Gln Ile Val Ser Tyr Gln Thr Arg Val Pro Pro Leu		
355	360	365
Thr Pro Cys Pro Ala Pro Cys Phe Cys Lys Thr His Pro Ser Asp Leu		
370	375	380
Gly Leu Ser Val Asn Cys Gln Glu Lys Asn Ile Gln Ser Met Ser Glu		
385	390	395
Leu Ile Pro Lys Pro Leu Asn Ala Lys Lys Leu His Val Asn Gly Asn		
405	410	415
Ser Ile Lys Asp Val Asp Val Ser Asp Phe Thr Asp Phe Glu Gly Leu		
420	425	430
Asp Leu Leu His Leu Gly Ser Asn Gln Ile Thr Val Ile Lys Gly Asp		
435	440	445
Val Phe His Asn Leu Thr Asn Leu Arg Arg Leu Tyr Leu Asn Gly Asn		
450	455	460
Gln Ile Glu Arg Leu Tyr Pro Glu Ile Phe Ser Gly Leu His Asn Leu		
465	470	475
Gln Tyr Leu Tyr Leu Glu Tyr Asn Leu Ile Lys Glu Ile Ser Ala Gly		
485	490	495
Thr Phe Asp Ser Met Pro Asn Leu Gln Leu Leu Tyr Leu Asn Asn Asn		
500	505	510
Leu Leu Lys Ser Leu Pro Val Tyr Ile Phe Ser Gly Ala Pro Leu Ala		
515	520	525
Arg Leu Asn Leu Arg Asn Asn Lys Phe Met Tyr Leu Pro Val Ser Gly		
530	535	540
Val Leu Asp Gln Leu Gln Ser Leu Thr Gln Ile Asp Leu Glu Gly Asn		
545	550	555
Pro Trp Asp Cys Thr Cys Asp Leu Val Ala Leu Lys Leu Trp Val Glu		
565	570	575
Lys Leu Ser Asp Gly Ile Val Val Lys Glu Leu Lys Cys Glu Thr Pro		
580	585	590
Val Gln Phe Ala Asn Ile Glu Leu Lys Ser Leu Lys Asn Glu Ile Leu		

595 600 605
 Cys Pro Lys Leu Leu Asn Lys Pro Ser Ala Pro Phe Thr Ser Pro Ala
 610 615 620
 Pro Ala Ile Thr Phe Thr Thr Pro Leu Gly Pro Ile Arg Ser Pro Pro
 625 630 635 640
 Gly Gly Pro Val Pro Leu Ser Ile Leu Ile Leu Ser Ile Leu Val Val
 645 650 655
 Leu Ile Leu Thr Val Phe Val Ala Phe Cys Leu Leu Val Phe Val Leu
 660 665 670
 Arg Arg Asn Lys Lys Pro Thr Val Lys His Glu Gly Leu Gly Asn Pro
 675 680 685
 Asp Cys Gly Ser Met Gln Leu Gln Leu Arg Lys His Asp His Lys Thr
 690 695 700
 Asn Lys Lys Asp Gly Leu Ser Thr Glu Ala Phe Ile Pro Gln Thr Ile
 705 710 715 720
 Glu Gln Met Ser Lys Ser His Thr Cys Gly Leu Lys Glu Ser Glu Thr
 725 730 735
 Gly Phe Met Phe Ser Asp Pro Pro Gly Gln Lys Val Val Met Arg Asn
 740 745 750
 Val Ala Asp Lys Glu Lys Asp Leu Leu His Val Asp Thr Arg Lys Arg
 755 760 765
 Leu Ser Thr Ile Asp Glu Leu Asp Glu Leu Phe Pro Ser Arg Asp Ser
 770 775 780
 Asn Val Phe Ile Gln Asn Phe Leu Glu Ser Lys Lys Glu Tyr Asn Ser
 785 790 795 800
 Ile Gly Val Ser Gly Phe Glu Ile Arg Tyr Pro Glu Lys Gln Pro Asp
 805 810 815
 Lys Lys Ser Lys Lys Ser Leu Ile Gly Gly Asn His Ser Lys Ile Val
 820 825 830
 Val Glu Gln Arg Lys Ser Glu Tyr Phe Glu Leu Lys Ala Lys Leu Gln
 835 840 845
 Ser Ser Pro Asp Tyr Leu Gln Val Leu Glu Glu Gln Thr Ala Leu Asn
 850 855 860
 Lys Ile
 865

<210> 33
 <211> 533
 <212> PRT
 <213> Homo sapiens

<400> 33

Met Ala Pro Gly Pro Phe Ser Ser Ala Leu Leu Ser Pro Pro Pro Ala
 1 5 10 15
 Ala Leu Pro Phe Leu Leu Leu Leu Trp Ala Gly Ala Ser Arg Gly Gln
 20 25 30
 Pro Cys Pro Gly Arg Cys Ile Cys Gln Asn Val Ala Pro Thr Leu Thr
 35 40 45
 Met Leu Cys Ala Lys Thr Gly Leu Leu Phe Val Pro Pro Ala Ile Asp
 50 55 60
 Arg Arg Val Val Glu Leu Arg Leu Thr Asp Asn Phe Ile Ala Ala Val
 65 70 75 80
 Arg Arg Arg Asp Phe Ala Asn Met Thr Ser Leu Val His Leu Thr Leu
 85 90 95
 Ser Arg Asn Thr Ile Gly Gln Val Ala Ala Gly Ala Phe Ala Asp Leu
 100 105 110
 Arg Ala Leu Arg Ala Leu His Leu Asp Ser Asn Arg Leu Ala Glu Val
 115 120 125
 Arg Gly Asp Gln Leu Arg Gly Leu Gly Asn Leu Arg His Leu Ile Leu
 130 135 140
 Gly Asn Asn Gln Ile Arg Arg Val Glu Ser Ala Ala Phe Asp Ala Phe
 145 150 155 160
 Leu Ser Thr Val Glu Asp Leu Asp Leu Ser Tyr Asn Asn Leu Glu Ala
 165 170 175
 Leu Pro Trp Glu Ala Val Gly Gln Met Val Asn Leu Asn Thr Leu Thr
 180 185 190
 Leu Asp His Asn Leu Ile Asp His Ile Ala Glu Gly Thr Phe Val Gln
 195 200 205
 Leu His Lys Leu Val Arg Leu Asp Met Thr Ser Asn Arg Leu His Lys
 210 215 220
 Leu Pro Pro Asp Gly Leu Phe Leu Arg Ser Gln Gly Thr Gly Pro Lys
 225 230 235 240
 Pro Pro Thr Pro Leu Thr Val Ser Phe Gly Gly Asn Pro Leu His Cys
 245 250 255
 Asn Cys Glu Leu Leu Trp Leu Arg Arg Leu Thr Arg Glu Asp Asp Leu
 260 265 270
 Glu Thr Cys Ala Thr Pro Glu His Leu Thr Asp Arg Tyr Phe Trp Ser
 275 280 285
 Ile Pro Glu Glu Glu Phe Leu Cys Glu Pro Pro Leu Ile Thr Arg Gln
 290 295 300
 Ala Gly Gly Arg Ala Leu Val Val Glu Gly Gln Ala Val Ser Leu Arg
 305 310 315 320
 Cys Arg Ala Val Gly Asp Pro Glu Pro Val Val His Trp Val Ala Pro
 325 330 335

Asp Gly Arg Leu Leu Gly Asn Ser Ser Arg Thr Arg Val Arg Gly Asp
 340 345 350
 Gly Thr Leu Asp Val Thr Ile Thr Thr Leu Arg Asp Ser Gly Thr Phe
 355 360 365
 Thr Cys Ile Ala Ser Asn Ala Ala Gly Glu Ala Thr Ala Pro Val Glu
 370 375 380
 Val Cys Val Val Pro Leu Pro Leu Met Ala Pro Pro Pro Ala Ala Pro
 385 390 395 400
 Pro Pro Leu Thr Glu Pro Gly Ser Ser Asp Ile Ala Thr Pro Gly Arg
 405 410 415
 Pro Gly Ala Asn Asp Ser Ala Ala Glu Arg Arg Leu Val Ala Ala Glu
 420 425 430
 Leu Thr Ser Asn Ser Val Leu Ile Arg Trp Pro Ala Gln Arg Pro Val
 435 440 445
 Pro Gly Ile Arg Met Tyr Gln Val Gln Tyr Asn Ser Ser Val Asp Asp
 450 455 460
 Ser Leu Val Tyr Ser Ser Ala Ser Leu Met His Ile Val Glu His Gln
 465 470 475 480
 Leu Asn Ala Ser Val Ile Cys Leu Ala Ser Pro Gly Asp Ala Ser Gly
 485 490 495
 Ala Gly Ala Val Ser Leu Pro Val Glu Ser Leu Ser Ser Trp Leu Ser
 500 505 510
 Asp Leu His Arg Glu Thr Cys Leu Leu Ala Ser Ile Ser Ala Phe Pro
 515 520 525
 Val Phe Ser Trp Pro
 530

<210> 34
 <211> 771
 <212> PRT
 <213> Homo sapiens

<400> 34
 Met Ala Pro Gly Pro Phe Ser Ser Ala Leu Leu Ser Pro Pro Pro Ala
 1 5 10 15
 Ala Leu Pro Phe Leu Leu Leu Leu Trp Ala Gly Ala Ser Arg Gly Gln
 20 25 30
 Pro Cys Pro Gly Arg Cys Ile Cys Gln Asn Val Ala Pro Thr Leu Thr
 35 40 45
 Met Leu Cys Ala Lys Thr Gly Leu Leu Phe Val Pro Pro Ala Ile Asp
 50 55 60
 Arg Arg Val Val Glu Leu Arg Leu Thr Asp Asn Phe Ile Ala Ala Val

65	70	75	80
Arg Arg Arg Asp Phe Ala Asn Met Thr Ser Leu Val His Leu Thr Leu			
85	90	95	
Ser Arg Asn Thr Ile Gly Gln Val Ala Ala Gly Ala Phe Ala Asp Leu			
100	105	110	
Arg Ala Leu Arg Ala Leu His Leu Asp Ser Asn Arg Leu Ala Glu Val			
115	120	125	
Arg Gly Asp Gln Leu Arg Gly Leu Gly Asn Leu Arg His Leu Ile Leu			
130	135	140	
Gly Asn Asn Gln Ile Arg Arg Val Glu Ser Ala Ala Phe Asp Ala Phe			
145	150	155	160
Leu Ser Thr Val Glu Asp Leu Asp Leu Ser Tyr Asn Asn Leu Glu Ala			
165	170	175	
Leu Pro Trp Glu Ala Val Gly Gln Met Val Asn Leu Asn Thr Leu Thr			
180	185	190	
Leu Asp His Asn Leu Ile Asp His Ile Ala Glu Gly Thr Phe Val Gln			
195	200	205	
Leu His Lys Leu Val Arg Leu Asp Met Thr Ser Asn Arg Leu His Lys			
210	215	220	
Leu Pro Pro Asp Gly Leu Phe Leu Arg Ser Gln Gly Thr Gly Pro Lys			
225	230	235	240
Pro Pro Thr Pro Leu Thr Val Ser Phe Gly Gly Asn Pro Leu His Cys			
245	250	255	
Asn Cys Glu Leu Leu Trp Leu Arg Arg Leu Thr Arg Glu Asp Asp Leu			
260	265	270	
Glu Thr Cys Ala Thr Pro Glu His Leu Thr Asp Arg Tyr Phe Trp Ser			
275	280	285	
Ile Pro Glu Glu Glu Phe Leu Cys Glu Pro Pro Leu Ile Thr Arg Gln			
290	295	300	
Ala Gly Gly Arg Ala Leu Val Val Glu Gly Gln Ala Val Ser Leu Arg			
305	310	315	320
Cys Arg Ala Val Gly Asp Pro Glu Pro Val Val His Trp Val Ala Pro			
325	330	335	
Asp Gly Arg Leu Leu Gly Asn Ser Ser Arg Thr Arg Val Arg Gly Asp			
340	345	350	
Gly Thr Leu Asp Val Thr Ile Thr Thr Leu Arg Asp Ser Gly Thr Phe			
355	360	365	
Thr Cys Ile Ala Ser Asn Ala Ala Gly Glu Ala Thr Ala Pro Val Glu			
370	375	380	
Val Cys Val Val Pro Leu Pro Leu Met Ala Pro Pro Pro Ala Ala Pro			
385	390	395	400
Pro Pro Leu Thr Glu Pro Gly Ser Ser Asp Ile Ala Thr Pro Gly Arg			

405	410	415
Pro Gly Ala Asn Asp Ser Ala Ala	Glu Arg Arg Leu Val Ala Ala Glu	
420	425	430
Leu Thr Ser Asn Ser Val Leu Ile Arg Trp Pro Ala Gln Arg Pro Val		
435	440	445
Pro Gly Ile Arg Met Tyr Gln Val Gln Tyr Asn Ser Ser Val Asp Asp		
450	455	460
Ser Leu Val Tyr Arg Met Ile Pro Ser Thr Ser Gln Thr Phe Leu Val		
465	470	475
Asn Asp Leu Ala Ala Gly Arg Ala Tyr Asp Leu Cys Val Leu Ala Val		
485	490	495
Tyr Asp Asp Gly Ala Thr Ala Leu Pro Ala Thr Arg Val Val Gly Cys		
500	505	510
Val Gln Phe Thr Thr Ala Gly Asp Pro Ala Pro Cys Arg Pro Leu Arg		
515	520	525
Ala His Phe Leu Gly Gly Thr Met Ile Ile Ala Ile Gly Gly Val Ile		
530	535	540
Val Ala Ser Val Leu Val Phe Ile Val Leu Leu Met Ile Arg Tyr Lys		
545	550	555
Val Tyr Gly Asp Gly Asp Ser Arg Arg Val Lys Gly Ser Arg Ser Leu		
565	570	575
Pro Arg Val Ser His Val Cys Ser Gln Thr Asn Gly Ala Gly Thr Gly		
580	585	590
Ala Ala Gln Ala Pro Ala Leu Pro Ala Gln Asp His Tyr Glu Ala Leu		
595	600	605
Arg Glu Val Glu Ser Gln Ala Ala Pro Ala Val Ala Val Glu Ala Lys		
610	615	620
Ala Met Glu Ala Glu Thr Ala Ser Ala Glu Pro Glu Val Val Leu Gly		
625	630	635
Arg Ser Leu Gly Gly Ser Ala Thr Ser Leu Cys Leu Leu Pro Ser Glu		
645	650	655
Glu Thr Ser Gly Glu Glu Ser Arg Ala Ala Val Gly Pro Arg Arg Ser		
660	665	670
Arg Ser Gly Ala Leu Glu Pro Pro Thr Ser Ala Pro Pro Thr Leu Ala		
675	680	685
Leu Val Pro Gly Gly Ala Ala Ala Arg Pro Arg Pro Gln Gln Arg Tyr		
690	695	700
Ser Phe Asp Gly Asp Tyr Gly Ala Leu Phe Gln Ser His Ser Tyr Pro		
705	710	715
Arg Arg Ala Arg Arg Thr Lys Arg His Arg Ser Thr Pro His Leu Asp		
725	730	735
Gly Ala Gly Gly Gly Ala Ala Gly Glu Asp Gly Asp Leu Gly Leu Gly		

740 745 750
 Ser Ala Arg Ala Cys Leu Ala Phe Thr Ser Thr Glu Trp Met Leu Glu
 755 760 765
 Ser Thr Val
 770

<210> 35
 <211> 399
 <212> PRT
 <213> Homo sapiens

<400> 35
 Met Trp Gln Leu Leu Ala Ala Ala Cys Trp Met Leu Leu Leu Gly Ser
 1 5 10 15
 Met Tyr Gly Tyr Asp Lys Lys Gly Asn Asn Ala Asn Pro Glu Ala Asn
 20 25 30
 Met Asn Ile Ser Gln Ile Ile Ser Tyr Trp Gly Tyr Pro Tyr Glu Glu
 35 40 45
 Tyr Asp Val Thr Thr Lys Asp Gly Tyr Ile Leu Gly Ile Tyr Arg Ile
 50 55 60
 Pro His Gly Arg Gly Cys Pro Gly Arg Thr Ala Pro Lys Pro Ala Val
 65 70 75 80
 Tyr Leu Gln His Gly Leu Ile Ala Ser Ala Ser Asn Trp Ile Cys Asn
 85 90 95
 Leu Pro Asn Asn Ser Leu Ala Phe Leu Leu Ala Asp Ser Gly Tyr Asp
 100 105 110
 Val Trp Leu Gly Asn Ser Arg Gly Asn Thr Trp Ser Arg Lys His Leu
 115 120 125
 Lys Leu Ser Pro Lys Ser Pro Glu Tyr Trp Ala Phe Ser Leu Asp Glu
 130 135 140
 Met Ala Lys Tyr Asp Leu Pro Ala Thr Ile Asn Phe Ile Ile Glu Lys
 145 150 155 160
 Thr Gly Gln Lys Arg Leu Tyr Tyr Val Gly His Ser Gln Gly Thr Thr
 165 170 175
 Ile Ala Phe Ile Ala Phe Ser Thr Asn Pro Glu Leu Ala Lys Lys Ile
 180 185 190
 Lys Ile Phe Phe Ala Leu Ala Pro Val Val Thr Val Lys Tyr Thr Gln
 195 200 205
 Ser Pro Met Lys Lys Leu Thr Thr Leu Ser Arg Arg Val Val Lys Val
 210 215 220
 Leu Phe Gly Asp Lys Met Phe His Pro His Thr Leu Phe Asp Gln Phe
 225 230 235 240

Ile Ala Thr Lys Val Cys Asn Arg Lys Leu Phe Arg Arg Ile Cys Ser
 245 250 255
 Asn Phe Leu Phe Thr Leu Ser Gly Phe Asp Pro Gln Asn Leu Asn Met
 260 265 270
 Ser Arg Leu Asp Val Tyr Leu Ser His Asn Pro Ala Gly Thr Ser Val
 275 280 285
 Gln Asn Met Leu His Trp Ala Gln Ala Val Asn Ser Gly Gln Leu Gln
 290 295 300
 Ala Phe Asp Trp Gly Asn Ser Asp Gln Asn Met Met His Phe His Gln
 305 310 315 320
 Leu Thr Pro Pro Leu Tyr Asn Ile Thr Lys Ile Glu Val Pro Thr Ala
 325 330 335
 Ile Trp Asn Gly Gly Gln Asp Ile Val Ala Asp Pro Lys Asp Val Glu
 340 345 350
 Asn Leu Leu Pro Gln Ile Ala Asn Leu Ile Tyr Tyr Lys Leu Ile Pro
 355 360 365
 His Tyr Asn His Val Asp Phe Tyr Leu Gly Glu Asp Ala Pro Gln Glu
 370 375 380
 Ile Tyr Gln Asp Leu Ile Ile Leu Met Glu Glu Tyr Leu Gln Asn
 385 390 395

<210> 36

<211> 255

<212> PRT

<213> Homo sapiens

<400> 36

Ile Val Gly Gly Ser Asn Ala Gln Pro Gly Thr Trp Pro Trp Gln Val
 1 5 10 15
 Ser Leu His His Gly Gly Gly His Ile Cys Gly Gly Ser Leu Ile Ala
 20 25 30
 Pro Ser Trp Val Leu Ser Ala Ala His Cys Phe Met Thr Gly Arg Gln
 35 40 45
 Tyr Arg Cys Pro Glu Thr Arg Arg Thr Arg Ser Ala Leu Pro Thr Arg
 50 55 60
 Lys Arg Arg Arg Ala Tyr Asn His Tyr Ser Gln Gly Ser Asp Leu Ala
 65 70 75 80
 Leu Leu Gln Leu Ala His Pro Thr Thr His Thr Pro Leu Cys Leu Pro
 85 90 95
 Gln Pro Ala His Arg Phe Pro Phe Gly Ala Ser Cys Trp Ala Thr Gly
 100 105 110
 Trp Asp Gln Asp Thr Ser Asp Ala Pro Ser Leu Ser Pro Ala Pro Gly

115 120 125
 Thr Leu Arg Asn Leu Arg Leu Arg Leu Ile Ser Arg Pro Thr Cys Asn
 130 135 140
 Cys Ile Tyr Asn Gln Leu His Gln Arg His Leu Ser Asn Pro Ala Arg
 145 150 155 160
 Pro Gly Met Leu Cys Gly Gly Pro Gln Pro Gly Val Gln Gly Pro Cys
 165 170 175
 Gln Gly Leu Phe Gly Ala Pro Leu Val His Glu Val Arg Gly Thr Trp
 180 185 190
 Phe Leu Ala Gly Leu His Ser Phe Gly Asp Ala Cys Gln Gly Pro Ala
 195 200 205
 Arg Pro Ala Val Phe Thr Ala Leu Pro Ala Met Arg Thr Gly Ser Ala
 210 215 220
 Val Trp Thr Arg Gln Val Tyr Phe Ala Glu Glu Pro Glu Pro Glu Ala
 225 230 235 240
 Glu Pro Gly Ser Cys Leu Ala Asn Ile Arg Pro Phe Ser Leu Gln
 245 250 255

<210> 37

<211> 301

<212> PRT

<213> Homo sapiens

<400> 37

Met Glu Thr Ala Gly Ser Asp Trp Val Ala Gly Gly Pro Leu Thr Gln
 1 5 10 15
 Ala Ser His Pro Ser Glu Cys Gly Lys Ala Pro Arg Pro Gly Ala Trp
 20 25 30
 Pro Trp Glu Ala Gln Val Met Val Pro Gly Ser Arg Pro Cys His Gly
 35 40 45
 Ala Leu Val Ser Glu Ser Trp Val Leu Ala Pro Ala Ser Cys Phe Leu
 50 55 60
 Glu Gln Val Thr His Thr Leu Cys Cys Cys Arg Met Thr Arg Val Gly
 65 70 75 80
 Ala Phe Cys Ala Arg Arg Arg Gly Pro Gly Phe Trp Leu Glu Ser Glu
 85 90 95
 Thr Phe Pro Val Ala Val Tyr Leu Pro Arg Ala Tyr Asn His Tyr Ser
 100 105 110
 Gln Gly Ser Asp Leu Ala Leu Leu Gln Leu Ala His Pro Thr Thr His
 115 120 125
 Thr Pro Leu Cys Leu Pro Gln Pro Ala His Arg Phe Pro Phe Gly Ala
 130 135 140

Ser Cys Trp Ala Thr Gly Trp Asp Gln Asp Thr Ser Asp Ala Pro Gly
 145 150 155 160
 Thr Leu Arg Asn Leu Arg Leu Arg Leu Ile Ser Arg Pro Thr Cys Asn
 165 170 175
 Cys Ile Tyr Asn Gln Leu His Gln Arg His Leu Ser Asn Pro Ala Arg
 180 185 190
 Pro Gly Met Leu Cys Gly Gly Pro Gln Pro Gly Val Gln Gly Pro Cys
 195 200 205
 Gln Gly Leu Phe Gly Ala Pro Leu Val His Glu Val Arg Gly Thr Trp
 210 215 220
 Phe Leu Ala Gly Leu His Ser Phe Gly Asp Ala Cys Gln Gly Pro Ala
 225 230 235 240
 Arg Pro Ala Val Phe Thr Ala Leu Pro Ala Met Arg Thr Gly Ser Ala
 245 250 255
 Val Trp Thr Arg Gln Val Tyr Phe Ala Glu Glu Pro Glu Pro Glu Ala
 260 265 270
 Glu Pro Gly Ser Cys Leu Ala Asn Ile Ser Met Trp Pro Arg Gly Leu
 275 280 285
 Leu Pro Asn Pro Ala Ser Pro Gly Pro Phe Ser Leu Gln
 290 295 300

<210> 38

<211> 383

<212> PRT

<213> Homo sapiens

<400> 38

Met Pro Ser Gly Cys Arg Cys Leu His Leu Val Cys Leu Leu Cys Ile
 1 5 10 15
 Leu Gly Ala Pro Gly Gln Pro Val Arg Ala Asp Asp Cys Ser Ser His
 20 25 30
 Cys Asp Leu Ala His Gly Cys Cys Ala Pro Asp Gly Ser Cys Arg Cys
 35 40 45
 Asp Pro Gly Trp Glu Gly Leu His Cys Glu Arg Cys Val Arg Met Pro
 50 55 60
 Gly Cys Gln His Gly Thr Cys His Gln Pro Trp Gln Cys Ile Cys His
 65 70 75 80
 Ser Gly Trp Ala Gly Lys Phe Cys Asp Lys Asp Glu His Ile Cys Thr
 85 90 95
 Thr Gln Ser Pro Cys Gln Asn Gly Gly Gln Cys Met Tyr Asp Gly Gly
 100 105 110
 Gly Glu Tyr His Cys Val Cys Leu Pro Gly Phe His Gly Arg Asp Cys

WO 01/66690

115 Glu Arg Lys Ala Gly Pro Cys Glu Gln Ala Gly Ser Pro Cys Arg Asn
 130 Gly Gly Gln Cys Gln Asp Asp Gln Gly Phe Ala Leu Asn Phe Thr Cys
 145 Arg Cys Leu Val Gly Phe Val Gly Ala Arg Cys Glu Val Asn Val Asp
 160 Asp Cys Leu Met Arg Pro Cys Ala Asn Gly Ala Thr Cys Leu Asp Gly
 175 Ile Asn Arg Phe Ser Cys Leu Cys Pro Glu Gly Phe Ala Gly Arg Phe
 190 Cys Thr Ile Asn Leu Asp Asp Cys Ala Ser Arg Pro Cys Gln Arg Gly
 205 Ala Arg Cys Arg Asp Arg Val His Asp Phe Asp Cys Leu Cys Pro Ser
 220 Gly Tyr Gly Gly Lys Thr Cys Glu Leu Val Leu Pro Val Pro Asp Pro
 235 Pro Thr Thr Val Asp Thr Pro Leu Gly Pro Thr Ser Ala Val Val Val
 250 Pro Ala Thr Gly Pro Ala Pro His Ser Ala Gly Ala Gly Leu Arg
 265 Ile Ser Val Lys Glu Val Val Phe Gly Ala Leu Thr Ala Ala Leu
 280 Pro Ser Leu Val Ala Leu Val Val Phe Gly Ala Leu Thr Ala Ala Leu
 300 Val Leu Ala Thr Val Leu Thr Leu Arg Ala Trp Arg Arg Gly Val
 315 Cys Pro Pro Gly Pro Cys Cys Tyr Pro Ala Pro His Tyr Ala Pro Ala
 330 Cys Gln Asp Gln Cys Glu Val Ser Met Leu Pro Ala Gly Leu Pro
 345 Leu Pro Arg Asp Leu Pro Pro Glu Pro Gly Lys Thr Thr Ala Leu
 360
 375

<210> 39

<211> 417

<212> PRT

<213> Homo sapiens

<400> 39

Met Ala Ser Tyr Leu Tyr Gly Val Leu Phe Ala Val Gly Leu Cys Ala

5

40/66

```

Pro Ile Tyr Cys Val Ser Pro Ala Asn Ala Pro Ser Ala Tyr Pro Arg
      20                      25                      30
Pro Ser Ser Thr Lys Ser Thr Pro Ala Ser Gln Val Tyr Ser Leu Asn
      35                      40                      45
Thr Asp Phe Ala Phe Arg Leu Tyr Arg Arg Leu Val Leu Glu Thr Pro
      50                      55                      60
Ser Gln Asn Ile Phe Phe Ser Pro Val Ser Val Ser Thr Ser Leu Ala
      65                      70                      75                      80
Met Leu Ser Leu Gly Ala His Ser Val Thr Lys Thr Gln Ile Leu Gln
      85                      90                      95
Gly Leu Gly Phe Asn Leu Thr His Thr Pro Glu Ser Ala Ile His Gln
      100                     105                     110
Gly Phe Gln His Leu Val His Ser Leu Thr Val Pro Ser Lys Asp Leu
      115                     120                     125
Thr Leu Lys Met Gly Ser Ala Leu Phe Val Lys Lys Glu Leu Gln Leu
      130                     135                     140
Gln Ala Asn Phe Leu Gly Asn Val Lys Arg Leu Tyr Glu Ala Glu Val
      145                     150                     155                     160
Phe Ser Thr Asp Phe Ser Asn Pro Ser Ile Ala Gln Ala Arg Ile Asn
      165                     170                     175
Ser His Val Lys Lys Lys Thr Gln Gly Lys Val Val Asp Ile Ile Gln
      180                     185                     190
Gly Leu Asp Leu Leu Thr Ala Met Val Leu Val Asn His Ile Phe Phe
      195                     200                     205
Lys Ala Lys Trp Glu Lys Pro Phe His Pro Glu Tyr Thr Arg Lys Asn
      210                     215                     220
Phe Pro Phe Leu Val Gly Glu Gln Val Thr Val His Val Pro Met Met
      225                     230                     235                     240
His Gln Lys Glu Gln Phe Ala Phe Gly Val Asp Thr Glu Leu Asn Cys
      245                     250                     255
Phe Val Leu Gln Met Asp Tyr Lys Gly Asp Ala Val Ala Phe Phe Val
      260                     265                     270
Leu Pro Ser Lys Gly Lys Met Arg Gln Leu Glu Gln Ala Leu Ser Ala
      275                     280                     285
Arg Thr Leu Arg Lys Trp Ser His Ser Leu Gln Lys Arg Trp Ile Glu
      290                     295                     300
Val Phe Ile Pro Arg Phe Ser Ile Ser Ala Ser Tyr Asn Leu Glu Thr
      305                     310                     315                     320
Ile Leu Pro Lys Met Gly Ile Gln Asn Val Phe Asp Lys Asn Ala Asp
      325                     330                     335
Phe Ser Gly Ile Ala Lys Arg Asp Ser Leu Gln Val Ser Lys Ala Thr
      340                     345                     350

```


His Lys Ala Val Leu Asp Val Ser Glu Glu Gly Thr Glu Ala Thr Ala
 355 360 365
 Ala Thr Thr Thr Lys Phe Ile Val Arg Ser Lys Asp Gly Pro Ser Tyr
 370 375 380
 Phe Thr Val Ser Phe Asn Arg Thr Phe Leu Met Met Ile Thr Asn Lys
 385 390 395 400
 Ala Thr Asp Gly Ile Leu Phe Leu Gly Lys Val Glu Asn Pro Thr Lys
 405 410 415
 Ser

<210> 40
 <211> 243
 <212> PRT
 <213> Homo sapiens

<400> 40
 Met Gly Ser Ser Ser Phe Leu Val Leu Met Val Ser Leu Val Leu Val
 1 5 10 15
 Thr Leu Val Ala Val Glu Gly Val Lys Glu Gly Ile Glu Lys Ala Gly
 20 25 30
 Val Cys Pro Ala Asp Asn Val Arg Cys Phe Lys Ser Asp Pro Pro Gln
 35 40 45
 Cys His Thr Asp Gln Asp Cys Leu Gly Glu Arg Lys Cys Cys Tyr Leu
 50 55 60
 His Cys Gly Phe Lys Cys Val Ile Pro Val Lys Glu Leu Glu Glu Gly
 65 70 75 80
 Gln Arg Leu Leu His Asn Arg Glu Leu Pro Pro Ala Ala Ile Leu Gly
 85 90 95
 Asp Ser Leu Thr Glu Lys Ser Gly Gly Cys Pro Pro Asp Asp Gly Pro
 100 105 110
 Cys Leu Leu Ser Val Pro Asp Gln Cys Val Glu Asp Ser Gln Cys Pro
 115 120 125
 Leu Thr Arg Lys Cys Cys Tyr Arg Ala Cys Phe Arg Gln Cys Val Pro
 130 135 140
 Arg Val Ser Gly Lys Cys Leu Pro Ser Thr Leu Leu Thr Ile Gln Ala
 145 150 155 160
 Pro Ser Phe Arg Ala Ser Gly Gln Gly Arg Ser Ser Pro Ser Ser Leu
 165 170 175
 Cys Cys Ser Glu Ala Gly Gln Leu Pro Arg Gly Pro Thr Ala Leu Pro
 180 185 190
 Gln Pro His Glu Pro Pro Val Ser Gln Gly Leu Arg Leu Leu Gly Gln

```

          195                200                205
Lys Ala Met Leu Pro Gln Arg Leu Arg Ala Gly Leu Pro Gly Ser Cys
      210                215                220
Gln Arg Tyr Gly Ser Trp Val Pro Arg Ala Gly Ala Ser Pro Leu Arg
225                230                235                240
Ala Gln Leu

```

```

<210> 41
<211> 185
<212> PRT
<213> Homo sapiens

```

```

      <400> 41
Met Gly Ser Ser Ser Phe Leu Val Leu Met Val Ser Leu Val Leu Val
  1                5                10                15
Thr Leu Val Ala Val Glu Gly Val Lys Glu Gly Ile Glu Lys Ala Gly
      20                25                30
Val Cys Pro Ala Asp Asn Val Arg Cys Phe Lys Ser Asp Pro Pro Gln
      35                40                45
Cys His Thr Asp Gln Asp Cys Leu Gly Glu Arg Lys Cys Cys Tyr Leu
      50                55                60
His Cys Gly Phe Lys Cys Val Ile Pro Val Lys Glu Leu Glu Glu Val
      65                70                75                80
Pro Cys Val Ala Val Lys Leu Gly Ser Cys Pro Glu Asp Gln Leu Arg
      85                90                95
Cys Leu Ser Pro Met Asn His Leu Cys His Lys Asp Ser Asp Cys Ser
      100                105                110
Gly Lys Lys Arg Cys Cys His Ser Ala Cys Gly Arg Asp Cys Arg Asp
      115                120                125
Pro Ala Arg Gly Thr Ala Pro Gly Cys Pro Gly Gln Val Pro Pro Leu
      130                135                140
Ser Glu Pro Ser Ser Asn Thr Phe Phe Ile Ala Thr Ser Leu Thr Gly
      145                150                155                160
Cys Leu Pro Arg Ser Gln Asp Leu Pro Trp Pro Gly Leu Gly Asn Trp
      165                170                175
Ile Gly Val Gly Gly Val Leu Leu Gly
      180                185

```

```

<210> 42
<211> 198
<212> PRT

```

<213> Homo sapiens

<400> 42

```

Met Asn Ser Gly Arg Glu Pro Arg Thr Pro Arg Thr Leu Leu Ser Ile
 1              5              10              15
Ala Asp Ile Leu Ala Pro Arg Met Val Pro Arg Ala Pro Ser Ala Pro
      20              25              30
Gln Leu Pro Glu Ser Gly Pro Gly Pro Thr Ser Pro Leu Cys Ala Leu
 35              40              45
Glu Glu Leu Thr Ser Lys Thr Phe Arg Gly Leu Asp Ala Arg Ala Leu
 50              55              60
Gln Pro Ser Glu Gly Arg Ala Gly Pro Asp Ala Leu Gly Pro Gly Pro
 65              70              75              80
Phe Gly Arg Lys Arg Arg Lys Ser Arg Thr Ala Phe Thr Ala Gln Gln
      85              90              95
Val Leu Glu Leu Glu Arg Arg Phe Val Phe Gln Lys Tyr Leu Ala Pro
      100              105              110
Ser Glu Arg Asp Gly Leu Ala Thr Arg Leu Gly Leu Ala Asn Ala Gln
      115              120              125
Val Val Thr Trp Phe Gln Asn Arg Arg Ala Lys Leu Lys Arg Asp Val
      130              135              140
Glu Glu Met Arg Ala Asp Val Ala Ser Leu Arg Ala Leu Ser Pro Glu
      145              150              155              160
Val Leu Cys Ser Leu Ala Leu Pro Glu Gly Ala Pro Asp Pro Gly Leu
      165              170              175
Cys Leu Gly Pro Ala Gly Pro Asp Ser Arg Pro His Leu Ser Asp Glu
      180              185              190
Glu Ile Gln Val Asp Asp
      195

```

<210> 43

<211> 330

<212> PRT

<213> Homo sapiens

<400> 43

```

Met Val Trp Lys Arg Glu Asn Phe Tyr Lys Glu Val Lys Arg Gly Arg
 1              5              10              15
Ala Leu Phe Leu Lys Arg Leu Cys Ile Phe Asn Ile Asp Thr Asp Asn
      20              25              30
Thr Phe Gln Arg Ile Ile Glu Lys Pro Ser Trp Leu Gly Phe Leu Gly
      35              40              45

```

```

Pro Met Ile Lys Ala Glu Thr Gly Asp Phe Ile Tyr Val His Val Lys
  50                      55                      60
Asn Asn Ala Ser Arg Ala Tyr Ser Tyr His Pro His Gly Leu Thr Tyr
  65                      70                      75                      80
Ser Lys Glu Asn Glu Gly Ala Ile Tyr Pro Asp Asn Thr Thr Gly Leu
                      85                      90                      95
Gln Lys Glu Asp Glu Tyr Leu Glu Pro Gly Lys Gln Tyr Thr Tyr Lys
                      100                      105                      110
Trp Tyr Val Glu Glu His Gln Gly Pro Gly Pro Asn Asp Ser Asn Cys
                      115                      120                      125
Val Thr Arg Ile Tyr His Ser His Ile Asp Thr Ala Arg Asp Val Ala
                      130                      135                      140
Ser Gly Leu Ile Gly Pro Ile Leu Thr Cys Lys Arg Ala Ile Asn Gly
  145                      150                      155                      160
Tyr Ile Tyr Gly Asn Leu Pro Asn Leu Thr Met Cys Ala Glu Asp Arg
                      165                      170                      175
Val Gln Trp Tyr Phe Val Gly Met Gly Gly Val Ala Asp Ile His Pro
                      180                      185                      190
Val Tyr Leu Arg Gly Gln Thr Leu Ile Ser Arg Asn His Arg Lys Asp
                      195                      200                      205
Thr Ile Met Leu Phe Pro Ser Ser Leu Glu Asp Ala Phe Met Val Ala
                      210                      215                      220
Lys Ala Pro Gly Val Trp Met Leu Gly Cys Gln Ile His Gly Ser Asp
  225                      230                      235                      240
Ile Leu Leu Leu Arg Asp Thr Lys Ser Glu Asn Phe Gln Gly Leu Ser
                      245                      250                      255
Pro Phe His Met His Phe Leu Thr Asn Glu Glu Thr Tyr Ile Gln Glu
                      260                      265                      270
Glu Ser Met Gln Ala Phe Phe Lys Val Ser Asn Cys Gln Lys Pro Ser
                      275                      280                      285
Thr Glu Ala Phe Val Thr Gly Thr His Val Ile His Tyr Tyr Ile Ala
                      290                      295                      300
Ala Lys Glu Ile Leu Trp Asn Tyr Ala Pro Ser Gly Ile Asp Phe Phe
  305                      310                      315                      320
Thr Lys Lys Asn Leu Thr Ala Ala Gly Arg
                      325                      330

```

<210> 44

<211> 479

<212> PRT

<213> Homo sapiens

<400> 44

```

Met Ala Ile Leu Pro Leu Leu Leu Cys Leu Leu Pro Leu Ala Pro Ala
 1              5              10              15
Ser Ser Pro Pro Gln Ser Ala Thr Pro Ser Pro Cys Pro Arg Arg Cys
      20              25              30
Arg Cys Gln Thr Gln Ser Leu Pro Leu Ser Val Leu Cys Pro Gly Ala
      35              40              45
Gly Leu Leu Phe Val Pro Pro Ser Leu Asp Arg Arg Ala Ala Glu Leu
 50              55              60
Arg Leu Ala Asp Asn Phe Ile Ala Ser Val Arg Arg Arg Asp Leu Ala
65              70              75              80
Asn Met Thr Gly Leu Leu His Leu Ser Leu Ser Arg Asn Thr Ile Arg
      85              90              95
His Val Ala Ala Gly Ala Phe Ala Asp Leu Arg Ala Leu Arg Ala Leu
      100             105             110
His Leu Asp Gly Asn Arg Leu Thr Ser Leu Gly Glu Gly Gln Leu Arg
      115             120             125
Gly Leu Val Asn Leu Arg His Leu Ile Leu Ser Asn Asn Gln Leu Ala
      130             135             140
Ala Leu Ala Ala Gly Ala Leu Asp Asp Cys Ala Glu Thr Leu Glu Asp
      145             150             155             160
Leu Asp Leu Ser Tyr Asn Asn Leu Glu Gln Leu Pro Trp Glu Ala Leu
      165             170             175
Gly Arg Leu Gly Asn Val Asn Thr Leu Gly Leu Asp His Asn Leu Leu
      180             185             190
Ala Ser Val Pro Ala Gly Ala Phe Ser Arg Leu His Lys Leu Ala Arg
      195             200             205
Leu Asp Met Thr Ser Asn Arg Leu Thr Thr Ile Pro Pro Asp Pro Leu
      210             215             220
Phe Ser Arg Leu Pro Leu Leu Ala Arg Pro Arg Gly Ser Pro Ala Ser
      225             230             235             240
Ala Leu Val Leu Ala Phe Gly Gly Asn Pro Leu His Cys Asn Cys Glu
      245             250             255
Leu Val Trp Leu Arg Arg Leu Ala Arg Glu Asp Asp Leu Glu Ala Cys
      260             265             270
Ala Ser Pro Pro Ala Leu Gly Gly Arg Tyr Phe Trp Ala Val Gly Glu
      275             280             285
Glu Glu Phe Val Cys Glu Pro Pro Val Val Thr His Arg Ser Pro Pro
      290             295             300
Leu Ala Val Pro Ala Gly Arg Pro Ala Ala Leu Arg Cys Arg Ala Val
      305             310             315             320
Gly Asp Pro Glu Pro Arg Val Arg Trp Val Ser Pro Gln Gly Arg Leu

```

	325		330		335
Leu Gly Asn Ser Ser Arg Ala Arg Ala Phe Pro Asn Gly Thr Leu Glu					
	340		345		350
Leu Leu Val Thr Glu Pro Gly Asp Gly Gly Ile Phe Thr Cys Ile Ala					
	355		360		365
Ala Asn Ala Ala Gly Glu Ala Thr Ala Ala Val Glu Leu Thr Val Gly					
	370		375		380
Pro Pro Pro Pro Pro Gln Leu Ala Asn Ser Thr Ser Cys Asp Pro Pro					
385		390		395	400
Arg Asp Gly Asp Pro Asp Ala Leu Thr Pro Pro Ser Ala Ala Ser Ala					
	405		410		415
Ser Ala Lys Val Ala Asp Thr Gly Pro Pro Thr Asp Arg Gly Val Gln					
	420		425		430
Val Thr Glu His Gly Ala Thr Ala Ala Leu Val Gln Trp Pro Asp Gln					
	435		440		445
Arg Pro Ile Pro Gly Ile Arg Met Tyr Gln Ile Gln Tyr Asn Ser Ser					
	450		455		460
Ala Asp Asp Ile Leu Val Tyr Arg Cys Arg Val Gln Ala Leu Gly					
465		470		475	

<210> 45

<211> 628

<212> PRT

<213> Homo sapiens

<400> 45

Met Ala Ile Leu Pro Leu Leu Leu Cys Leu Leu Pro Leu Ala Pro Ala			
1	5	10	15
Ser Ser Pro Pro Gln Ser Ala Thr Pro Ser Pro Cys Pro Arg Arg Cys			
	20	25	30
Arg Cys Gln Thr Gln Ser Leu Pro Leu Ser Val Leu Cys Pro Gly Ala			
	35	40	45
Gly Leu Leu Phe Val Pro Pro Ser Leu Asp Arg Arg Ala Ala Glu Leu			
	50	55	60
Arg Leu Ala Asp Asn Phe Ile Ala Ser Val Arg Arg Arg Asp Leu Ala			
65		70	75
Asn Met Thr Gly Leu Leu His Leu Ser Leu Ser Arg Asn Thr Ile Arg			
	85	90	95
His Val Ala Ala Gly Ala Phe Ala Asp Leu Arg Ala Leu Arg Ala Leu			
	100	105	110
His Leu Asp Gly Asn Arg Leu Thr Ser Leu Gly Glu Gly Gln Leu Arg			
	115	120	125

Gly Leu Val Asn Leu Arg His Leu Ile Leu Ser Asn Asn Gln Leu Ala
 130 135 140
 Ala Leu Ala Ala Gly Ala Leu Asp Asp Cys Ala Glu Thr Leu Glu Asp
 145 150 155 160
 Leu Asp Leu Ser Tyr Asn Asn Leu Glu Gln Leu Pro Trp Glu Ala Leu
 165 170 175
 Gly Arg Leu Gly Asn Val Asn Thr Leu Gly Leu Asp His Asn Leu Leu
 180 185 190
 Ala Ser Val Pro Ala Gly Ala Phe Ser Arg Leu His Lys Leu Ala Arg
 195 200 205
 Leu Asp Met Thr Ser Asn Arg Leu Thr Thr Ile Pro Pro Asp Pro Leu
 210 215 220
 Phe Ser Arg Leu Pro Leu Leu Ala Arg Pro Arg Gly Ser Pro Ala Ser
 225 230 235 240
 Ala Leu Val Leu Ala Phe Gly Gly Asn Pro Leu His Cys Asn Cys Glu
 245 250 255
 Leu Val Trp Leu Arg Arg Leu Ala Arg Glu Asp Asp Leu Glu Ala Cys
 260 265 270
 Ala Ser Pro Pro Ala Leu Gly Gly Arg Tyr Phe Trp Ala Val Gly Glu
 275 280 285
 Glu Glu Phe Val Cys Glu Pro Pro Val Val Thr His Arg Ser Pro Pro
 290 295 300
 Leu Ala Val Pro Ala Gly Arg Pro Ala Ala Leu Arg Cys Arg Ala Val
 305 310 315 320
 Gly Asp Pro Glu Pro Arg Val Arg Trp Val Ser Pro Gln Gly Arg Leu
 325 330 335
 Leu Gly Asn Ser Ser Arg Ala Arg Ala Phe Pro Asn Gly Thr Leu Glu
 340 345 350
 Leu Leu Val Thr Glu Pro Gly Asp Gly Gly Ile Phe Thr Cys Ile Ala
 355 360 365
 Ala Asn Ala Ala Gly Glu Ala Thr Ala Ala Val Glu Leu Thr Val Gly
 370 375 380
 Pro Pro Pro Pro Pro Gln Leu Ala Asn Ser Thr Ser Cys Asp Pro Pro
 385 390 395 400
 Arg Asp Gly Asp Pro Asp Ala Leu Thr Pro Pro Ser Ala Ala Ser Ala
 405 410 415
 Ser Ala Lys Val Ala Asp Thr Gly Pro Pro Thr Asp Arg Gly Val Gln
 420 425 430
 Val Thr Glu His Gly Ala Thr Ala Ala Leu Val Gln Trp Pro Asp Gln
 435 440 445
 Arg Pro Ile Pro Gly Ile Arg Met Tyr Gln Ile Gln Tyr Asn Ser Ser
 450 455 460

Ala Asp Asp Ile Leu Val Tyr Arg Met Ile Pro Ala Glu Ser Arg Ser
 465 470 475 480
 Phe Leu Leu Thr Asp Leu Ala Ser Gly Arg Thr Tyr Asp Leu Cys Val
 485 490 495
 Leu Ala Val Tyr Glu Asp Ser Ala Thr Gly Leu Thr Ala Thr Arg Pro
 500 505 510
 Val Gly Cys Ala Arg Phe Ser Thr Glu Pro Ala Leu Arg Pro Cys Gly
 515 520 525
 Ala Pro His Ala Pro Phe Leu Gly Gly Thr Met Ile Ile Ala Leu Gly
 530 535 540
 Gly Val Ile Val Ala Ser Val Leu Val Phe Ile Phe Val Leu Leu Met
 545 550 555 560
 Arg Tyr Lys Val His Gly Gly Gln Pro Pro Gly Lys Ala Lys Ile Pro
 565 570 575
 Ala Pro Val Ser Ser Val Cys Ser Gln Thr Asn Gly Ala Leu Gly Pro
 580 585 590
 Thr Pro Thr Pro Ala Pro Pro Ala Pro Glu Pro Ala Ala Leu Arg Ala
 595 600 605
 His Thr Val Val Gln Leu Asp Cys Glu Pro Trp Gly Pro Gly His Glu
 610 615 620
 Pro Val Gly Pro
 625

<210> 46
 <211> 845
 <212> PRT
 <213> Homo sapiens

<400> 46
 Met Leu Ser Gly Val Trp Phe Leu Ser Val Leu Thr Val Ala Gly Ile
 1 5 10 15
 Leu Gln Thr Glu Ser Arg Lys Thr Ala Lys Asp Ile Cys Lys Ile Arg
 20 25 30
 Cys Leu Cys Glu Glu Lys Glu Asn Val Leu Asn Ile Asn Cys Glu Asn
 35 40 45
 Lys Gly Phe Thr Thr Val Ser Leu Leu Gln Pro Pro Gln Tyr Arg Ile
 50 55 60
 Tyr Gln Leu Phe Leu Asn Gly Asn Leu Leu Thr Arg Leu Tyr Pro Asn
 65 70 75 80
 Glu Phe Val Asn Tyr Ser Asn Ala Val Thr Leu His Leu Gly Asn Asn
 85 90 95
 Gly Leu Gln Glu Ile Arg Thr Gly Ala Phe Ser Gly Leu Lys Thr Leu

100	105	110
Lys Arg Leu His Leu Asn Asn Asn Lys Leu Glu Ile Leu Arg Glu Asp		
115	120	125
Thr Phe Leu Gly Leu Glu Ser Leu Glu Tyr Leu Gln Ala Asp Tyr Asn		
130	135	140
Tyr Ile Ser Ala Ile Glu Ala Gly Ala Phe Ser Lys Leu Asn Lys Leu		
145	150	155
Lys Val Leu Ile Leu Asn Asp Asn Leu Leu Leu Ser Leu Pro Ser Asn		
165	170	175
Val Phe Arg Phe Val Leu Leu Thr His Leu Asp Leu Arg Gly Asn Arg		
180	185	190
Leu Lys Val Met Pro Phe Ala Gly Val Leu Glu His Ile Gly Gly Ile		
195	200	205
Met Glu Ile Gln Leu Glu Glu Asn Pro Trp Asn Cys Thr Cys Asp Leu		
210	215	220
Leu Pro Leu Lys Ala Trp Leu Asp Thr Ile Thr Val Phe Val Gly Glu		
225	230	235
Ile Val Cys Glu Thr Pro Phe Arg Leu His Gly Lys Asp Val Thr Gln		
245	250	255
Leu Thr Arg Gln Asp Leu Cys Pro Arg Lys Ser Ala Ser Asp Ser Ser		
260	265	270
Gln Arg Gly Ser His Ala Asp Thr His Val Gln Arg Leu Ser Pro Thr		
275	280	285
Met Asn Pro Ala Leu Asn Pro Thr Arg Ala Pro Lys Ala Ser Arg Pro		
290	295	300
Pro Lys Met Arg Asn Arg Pro Thr Pro Arg Val Thr Val Ser Lys Asp		
305	310	315
Arg Gln Ser Phe Gly Pro Ile Met Val Tyr Gln Thr Lys Ser Pro Val		
325	330	335
Pro Leu Thr Cys Pro Ser Ser Cys Val Cys Thr Ser Gln Ser Ser Asp		
340	345	350
Asn Gly Leu Asn Val Asn Cys Gln Glu Arg Lys Phe Thr Asn Ile Ser		
355	360	365
Asp Leu Gln Pro Lys Pro Thr Ser Pro Lys Lys Leu Tyr Leu Thr Gly		
370	375	380
Asn Tyr Leu Gln Thr Val Tyr Lys Asn Asp Leu Leu Glu Tyr Ser Ser		
385	390	395
Leu Asp Leu Leu His Leu Gly Asn Asn Arg Ile Ala Val Ile Gln Glu		
405	410	415
Gly Ala Phe Thr Asn Leu Thr Ser Leu Arg Arg Leu Tyr Leu Asn Gly		
420	425	430
Asn Tyr Leu Glu Val Leu Tyr Pro Ser Met Phe Asp Gly Leu Gln Ser		

```

      435              440              445
Leu Gln Tyr Leu Tyr Leu Glu Tyr Asn Val Ile Lys Glu Ile Lys Pro
      450              455              460
Leu Thr Phe Asp Ala Leu Ile Asn Leu Gln Leu Leu Phe Leu Asn Asn
465              470              475              480
Asn Leu Leu Arg Ser Leu Pro Asp Asn Ile Phe Gly Gly Thr Ala Leu
      485              490              495
Thr Arg Leu Asn Leu Arg Asn Asn His Phe Ser His Leu Pro Val Lys
      500              505              510
Gly Val Leu Asp Gln Leu Pro Ala Phe Ile Gln Ile Asp Leu Gln Glu
      515              520              525
Asn Pro Trp Asp Cys Thr Cys Asp Ile Met Gly Leu Lys Asp Trp Thr
      530              535              540
Glu His Ala Asn Ser Pro Val Ile Ile Asn Glu Val Thr Cys Glu Ser
545              550              555              560
Pro Ala Lys His Ala Gly Glu Ile Leu Lys Phe Leu Gly Arg Glu Ala
      565              570              575
Ile Cys Pro Asp Ser Pro Asn Leu Ser Asp Gly Thr Val Leu Ser Met
      580              585              590
Asn His Asn Thr Asp Thr Pro Arg Ser Leu Ser Val Ser Pro Ser Ser
      595              600              605
Tyr Pro Glu Leu His Thr Glu Val Pro Leu Ser Val Leu Ile Leu Gly
      610              615              620
Leu Leu Val Val Phe Ile Leu Ser Val Cys Phe Gly Ala Gly Leu Phe
625              630              635              640
Val Phe Val Leu Lys Arg Arg Lys Gly Val Pro Ser Val Pro Arg Asn
      645              650              655
Thr Asn Asn Leu Asp Val Ser Ser Phe Gln Leu Gln Tyr Gly Ser Tyr
      660              665              670
Asn Thr Glu Thr His Asp Lys Thr Asp Gly His Val Tyr Asn Tyr Ile
      675              680              685
Pro Pro Pro Val Gly Gln Met Cys Gln Asn Pro Ile Tyr Met Gln Lys
      690              695              700
Glu Gly Asp Pro Val Ala Tyr Tyr Arg Asn Leu Gln Glu Phe Ser Tyr
705              710              715              720
Ser Asn Leu Glu Glu Lys Lys Glu Glu Pro Ala Thr Pro Ala Tyr Thr
      725              730              735
Ile Ser Ala Thr Glu Leu Leu Glu Lys Gln Ala Thr Pro Arg Glu Pro
      740              745              750
Glu Leu Leu Tyr Gln Asn Ile Ala Glu Arg Val Lys Glu Leu Pro Ser
      755              760              765
Ala Gly Leu Val His Tyr Asn Phe Cys Thr Leu Pro Lys Arg Gln Phe

```

770	775	780
Ala Pro Ser Tyr Glu Ser Arg Arg Gln Asn Gln Asp Arg Ile Asn Lys		
785	790	795
Thr Val Leu Tyr Gly Thr Pro Arg Lys Cys Phe Val Gly Gln Ser Lys		
805	810	815
Pro Asn His Pro Leu Leu Gln Ala Lys Pro Gln Ser Glu Pro Asp Tyr		
820	825	830
Leu Glu Val Leu Glu Lys Gln Thr Ala Ile Ser Gln Leu		
835	840	845

<210> 47

<211> 349

<212> PRT

<213> Homo sapiens

<400> 47

Met Gly Ile Thr Cys Trp Ile Ala Leu Tyr Ala Val Glu Ala Leu Pro		
1	5	10
Thr Cys Pro Phe Ser Cys Lys Cys Asp Ser Arg Ser Leu Glu Val Asp		
20	25	30
Cys Ser Gly Leu Gly Leu Thr Thr Val Pro Pro Asp Val Pro Ala Ala		
35	40	45
Thr Arg Thr Leu Leu Leu Leu Asn Asn Lys Leu Ser Ala Leu Pro Ser		
50	55	60
Trp Ala Phe Ala Asn Leu Ser Ser Leu Gln Arg Leu Asp Leu Ser Asn		
65	70	75
Asn Phe Leu Asp Arg Leu Pro Arg Ser Ile Phe Gly Asp Leu Thr Asn		
85	90	95
Leu Thr Glu Leu Gln Leu Arg Asn Asn Ser Ile Arg Thr Leu Asp Arg		
100	105	110
Asp Leu Leu Arg His Ser Pro Leu Leu Arg His Leu Asp Leu Ser Ile		
115	120	125
Asn Gly Leu Ala Gln Leu Pro Pro Gly Leu Phe Asp Gly Leu Leu Ala		
130	135	140
Leu Arg Ser Leu Ser Leu Arg Ser Asn Arg Leu Gln Asn Leu Asp Arg		
145	150	155
Leu Thr Phe Glu Pro Leu Ala Asn Leu Gln Leu Leu Gln Val Gly Asp		
165	170	175
Asn Pro Trp Glu Cys Asp Cys Asn Leu Arg Glu Phe Lys His Trp Met		
180	185	190
Glu Trp Phe Ser Tyr Arg Gly Gly Arg Leu Asp Gln Leu Ala Cys Thr		
195	200	205

Leu Pro Lys Glu Leu Arg Gly Lys Asp Met Arg Met Val Pro Met Glu
 210 215 220
 Met Phe Asn Tyr Cys Ser Gln Leu Glu Asp Glu Asn Ser Ser Ala Gly
 225 230 235 240
 Leu Asp Ile Pro Gly Pro Pro Cys Thr Lys Ala Ser Pro Glu Pro Ala
 245 250 255
 Lys Pro Lys Pro Gly Ala Glu Pro Glu Pro Glu Pro Ser Thr Ala Cys
 260 265 270
 Pro Gln Lys Gln Arg His Arg Pro Ala Ser Val Arg Arg Ala Met Gly
 275 280 285
 Thr Val Ile Ile Ala Gly Val Val Cys Gly Val Val Cys Ile Met Met
 290 295 300
 Val Val Ala Ala Ala Tyr Gly Cys Ile Tyr Ala Ser Leu Met Ala Lys
 305 310 315 320
 Tyr His Arg Glu Leu Lys Lys Arg Gln Pro Leu Met Gly Asp Pro Glu
 325 330 335
 Gly Glu His Glu Asp Gln Lys Gln Ile Ser Ser Val Ala
 340 345

<210> 48
 <211> 738
 <212> PRT
 <213> Homo sapiens

<400> 48

Met Gly Met Thr Val Ile Lys Gln Ile Thr Asp Asp Leu Phe Val Trp
 1 5 10 15
 Asn Val Leu Asn Arg Glu Glu Val Asn Ile Ile Cys Cys Glu Lys Val
 20 25 30
 Glu Gln Asp Ala Ala Arg Gly Ile Ile His Met Ile Leu Lys Lys Gly
 35 40 45
 Ser Glu Ser Cys Asn Leu Phe Leu Lys Ser Leu Lys Glu Trp Asn Tyr
 50 55 60
 Pro Leu Phe Gln Asp Leu Asn Gly Gln Ser Leu Phe His Gln Thr Ser
 65 70 75 80
 Glu Gly Asp Leu Asp Asp Leu Ala Gln Asp Leu Lys Asp Leu Tyr His
 85 90 95
 Thr Pro Ser Phe Leu Asn Phe Tyr Pro Leu Gly Glu Asp Ile Asp Ile
 100 105 110
 Ile Phe Asn Leu Lys Ser Thr Phe Thr Glu Pro Val Leu Trp Arg Lys
 115 120 125
 Asp Gln His His His Arg Val Glu Gln Leu Thr Leu Asn Gly Leu Leu

130	135	140			
Gln Ala Leu Gln Ser Pro Cys Ile Ile Glu Gly Glu Ser Gly Lys Gly					
145	150	155	160		
Lys Ser Thr Leu Leu Gln Arg Ile Ala Met Leu Trp Gly Ser Gly Lys					
	165	170	175		
Cys Lys Ala Leu Thr Lys Phe Lys Phe Val Phe Phe Leu Arg Leu Ser					
	180	185	190		
Arg Ala Gln Gly Gly Leu Phe Glu Thr Leu Cys Asp Gln Leu Leu Asp					
	195	200	205		
Ile Pro Gly Thr Ile Arg Lys Gln Thr Phe Met Ala Met Leu Leu Lys					
	210	215	220		
Leu Arg Gln Arg Val Leu Phe Leu Leu Asp Gly Tyr Asn Glu Phe Lys					
225	230	235	240		
Pro Gln Asn Cys Pro Glu Ile Glu Ala Leu Ile Lys Glu Asn His Arg					
	245	250	255		
Phe Lys Asn Met Val Ile Val Thr Thr Thr Thr Glu Cys Leu Arg His					
	260	265	270		
Ile Arg Gln Phe Gly Ala Leu Thr Ala Glu Val Gly Asp Met Thr Glu					
	275	280	285		
Asp Ser Ala Gln Ala Leu Ile Arg Glu Val Leu Ile Lys Glu Leu Ala					
	290	295	300		
Glu Gly Leu Leu Leu Gln Ile Gln Lys Ser Arg Cys Leu Arg Asn Leu					
305	310	315	320		
Met Lys Thr Pro Leu Phe Val Val Ile Thr Cys Ala Ile Gln Met Gly					
	325	330	335		
Glu Ser Glu Phe His Ser His Thr Gln Thr Thr Leu Phe His Thr Phe					
	340	345	350		
Tyr Asp Leu Leu Ile Gln Lys Asn Lys His Lys His Lys Gly Val Ala					
	355	360	365		
Ala Ser Asp Phe Ile Arg Ser Leu Asp His Cys Gly Asp Leu Ala Leu					
	370	375	380		
Glu Gly Val Phe Ser His Lys Phe Asp Phe Glu Leu Gln Asp Val Ser					
385	390	395	400		
Ser Val Asn Glu Asp Val Leu Leu Thr Thr Gly Leu Leu Cys Lys Tyr					
	405	410	415		
Thr Ala Gln Arg Phe Lys Pro Lys Tyr Lys Phe Phe His Lys Ser Phe					
	420	425	430		
Gln Glu Tyr Thr Ala Gly Arg Arg Leu Ser Ser Leu Leu Thr Ser His					
	435	440	445		
Glu Pro Glu Glu Val Thr Lys Gly Asn Gly Tyr Leu Gln Lys Met Val					
450	455	460			
Ser Ile Ser Asp Ile Thr Ser Thr Tyr Ser Ser Leu Leu Arg Tyr Thr					

465 470 475 480
 Cys Gly Ser Ser Val Glu Ala Thr Arg Ala Val Met Lys His Leu Ala
 485 490 495
 Ala Val Tyr Gln His Gly Cys Leu Leu Gly Leu Ser Ile Ala Lys Arg
 500 505 510
 Pro Leu Trp Arg Gln Glu Ser Leu Gln Ser Val Lys Asn Thr Thr Glu
 515 520 525
 Gln Glu Ile Leu Lys Ala Ile Asn Ile Asn Ser Phe Val Glu Cys Gly
 530 535 540
 Ile His Leu Tyr Gln Glu Ser Thr Ser Lys Ser Ala Leu Ser Gln Glu
 545 550 555 560
 Phe Glu Ala Phe Phe Gln Gly Lys Ser Leu Tyr Ile Asn Ser Gly Asn
 565 570 575
 Ile Pro Asp Tyr Leu Phe Asp Phe Phe Glu His Leu Pro Asn Cys Ala
 580 585 590
 Ser Ala Leu Asp Phe Ile Lys Leu Asp Phe Tyr Gly Gly Ala Met Ala
 595 600 605
 Ser Trp Glu Lys Ala Ala Glu Asp Thr Gly Gly Ile His Met Glu Glu
 610 615 620
 Ala Pro Glu Thr Tyr Ile Pro Ser Arg Ala Val Ser Leu Phe Phe Asn
 625 630 635 640
 Trp Lys Gln Glu Phe Arg Thr Leu Glu Val Thr Leu Arg Asp Phe Ser
 645 650 655
 Lys Leu Asn Lys Gln Asp Ile Arg Tyr Leu Gly Lys Ile Phe Ser Ser
 660 665 670
 Ala Thr Ser Leu Arg Leu Gln Ile Lys Arg Cys Ala Gly Val Ala Gly
 675 680 685
 Ser Leu Ser Leu Val Leu Ser Thr Cys Lys Asn Ile Tyr Ser Leu Met
 690 695 700
 Val Glu Ala Ser Pro Leu Thr Ile Glu Asp Glu Arg His Ile Thr Ser
 705 710 715 720
 Val Thr Asn Leu Lys Thr Leu Ser Ile His Asp Leu Gln Asn Gln Arg
 725 730 735
 Leu Pro

<210> 49

<211> 1070

<212> PRT

<213> Homo sapiens

<400> 49

Met Tyr Lys Ser Leu Asn Ile Asp Glu Cys Asp Leu His Ala Trp Leu
 1 5 10 15
 Asp Leu Pro Ala Glu Lys Pro Leu Gly Val Val Asn Arg Val Cys Trp
 20 25 30
 Gly Phe Ile Arg Phe Lys Gly Tyr Met Tyr Pro Leu Asp Tyr Leu Asn
 35 40 45
 Phe Ile Lys Asp Asn Ser Arg Ala Leu Ile Gln Arg Met Gly Met Thr
 50 55 60
 Val Ile Lys Gln Ile Thr Asp Asp Leu Phe Val Trp Asn Val Leu Asn
 65 70 75 80
 Arg Glu Glu Val Asn Ile Ile Cys Cys Glu Lys Val Glu Gln Asp Ala
 85 90 95
 Ala Arg Gly Ile Ile His Met Ile Leu Lys Lys Gly Ser Glu Ser Cys
 100 105 110
 Asn Leu Phe Leu Lys Ser Leu Lys Glu Trp Asn Tyr Pro Leu Phe Gln
 115 120 125
 Asp Leu Asn Gly Gln Ser Leu Phe His Gln Thr Ser Glu Gly Asp Leu
 130 135 140
 Asp Asp Leu Ala Gln Asp Leu Lys Asp Leu Tyr His Thr Pro Ser Phe
 145 150 155 160
 Leu Asn Phe Tyr Pro Leu Gly Glu Asp Ile Asp Ile Ile Phe Asn Leu
 165 170 175
 Lys Ser Thr Phe Thr Glu Pro Val Leu Trp Arg Lys Asp Gln His His
 180 185 190
 His Arg Val Glu Gln Leu Thr Leu Asn Gly Leu Leu Gln Ala Leu Gln
 195 200 205
 Ser Pro Cys Ile Ile Glu Gly Glu Ser Gly Lys Gly Lys Ser Thr Leu
 210 215 220
 Leu Gln Arg Ile Ala Met Leu Trp Gly Ser Gly Lys Cys Lys Ala Leu
 225 230 235 240
 Thr Lys Phe Lys Phe Val Phe Phe Leu Arg Leu Ser Arg Ala Gln Gly
 245 250 255
 Gly Leu Phe Glu Thr Leu Cys Asp Gln Leu Leu Asp Ile Pro Gly Thr
 260 265 270
 Ile Arg Lys Gln Thr Phe Met Ala Met Leu Leu Lys Leu Arg Gln Arg
 275 280 285
 Val Leu Phe Leu Leu Asp Gly Tyr Asn Glu Phe Lys Pro Gln Asn Cys
 290 295 300
 Pro Glu Ile Glu Ala Leu Ile Lys Glu Asn His Arg Phe Lys Asn Met
 305 310 315 320
 Val Ile Val Thr Thr Thr Thr Glu Cys Leu Arg His Ile Arg Gln Phe
 325 330 335

Gly Ala Leu Thr Ala Glu Val Gly Asp Met Thr Glu Asp Ser Ala Gln
 340 345 350
 Ala Leu Ile Arg Glu Val Leu Ile Lys Glu Leu Ala Glu Gly Leu Leu
 355 360 365
 Leu Gln Ile Gln Lys Ser Arg Cys Leu Arg Asn Leu Met Lys Thr Pro
 370 375 380
 Leu Phe Val Val Ile Thr Cys Ala Ile Gln Met Gly Glu Ser Glu Phe
 385 390 395 400
 His Ser His Thr Gln Thr Thr Leu Phe His Thr Phe Tyr Asp Leu Leu
 405 410 415
 Ile Gln Lys Asn Lys His Lys His Lys Gly Val Ala Ala Ser Asp Phe
 420 425 430
 Ile Arg Ser Leu Asp His Cys Gly Asp Leu Ala Leu Glu Gly Val Phe
 435 440 445
 Ser His Lys Phe Asp Phe Glu Leu Gln Asp Val Ser Ser Val Asn Glu
 450 455 460
 Asp Val Leu Leu Thr Thr Gly Leu Leu Cys Lys Tyr Thr Ala Gln Arg
 465 470 475 480
 Phe Lys Pro Lys Tyr Lys Phe Phe His Lys Ser Phe Gln Glu Tyr Thr
 485 490 495
 Ala Gly Arg Arg Leu Ser Ser Leu Leu Thr Ser His Glu Pro Glu Glu
 500 505 510
 Val Thr Lys Gly Asn Gly Tyr Leu Gln Lys Met Val Ser Ile Ser Asp
 515 520 525
 Ile Thr Ser Thr Tyr Ser Ser Leu Leu Arg Tyr Thr Cys Gly Ser Ser
 530 535 540
 Val Glu Ala Thr Arg Ala Val Met Lys His Leu Ala Ala Val Tyr Gln
 545 550 555 560
 His Gly Cys Leu Leu Gly Leu Ser Ile Ala Lys Arg Pro Leu Trp Arg
 565 570 575
 Gln Glu Ser Leu Gln Ser Val Lys Asn Thr Thr Glu Gln Glu Ile Leu
 580 585 590
 Lys Ala Ile Asn Ile Asn Ser Phe Val Glu Cys Gly Ile His Leu Tyr
 595 600 605
 Gln Glu Ser Thr Ser Lys Ser Ala Leu Ser Gln Glu Phe Glu Ala Phe
 610 615 620
 Phe Gln Gly Lys Ser Leu Tyr Ile Asn Ser Gly Asn Ile Pro Asp Tyr
 625 630 635 640
 Leu Phe Asp Phe Phe Glu His Leu Pro Asn Cys Ala Ser Ala Leu Asp
 645 650 655
 Phe Ile Lys Leu Asp Phe Tyr Gly Gly Ala Met Ala Ser Trp Glu Lys
 660 665 670

Ala Ala Glu Asp Thr Gly Gly Ile His Met Glu Glu Ala Pro Glu Thr
 675 680 685
 Tyr Ile Pro Ser Arg Ala Val Ser Leu Phe Phe Asn Trp Lys Gln Glu
 690 695 700
 Phe Arg Thr Leu Glu Val Thr Leu Arg Asp Phe Ser Lys Leu Asn Lys
 705 710 715 720
 Gln Asp Ile Arg Tyr Leu Gly Lys Ile Phe Ser Ser Ala Thr Ser Leu
 725 730 735
 Arg Leu Gln Ile Lys Arg Cys Ala Gly Val Ala Gly Ser Leu Ser Leu
 740 745 750
 Val Leu Ser Thr Cys Lys Asn Ile Tyr Ser Leu Met Val Glu Ala Ser
 755 760 765
 Pro Leu Thr Ile Glu Asp Glu Arg His Ile Thr Ser Val Thr Asn Leu
 770 775 780
 Lys Thr Leu Ser Ile His Asp Leu Gln Asn Gln Arg Leu Pro Gly Gly
 785 790 795 800
 Leu Thr Asp Ser Leu Gly Asn Leu Lys Asn Leu Thr Lys Leu Ile Met
 805 810 815
 Asp Asn Ile Lys Met Asn Glu Glu Asp Ala Ile Lys Leu Ala Glu Gly
 820 825 830
 Leu Lys Asn Leu Lys Lys Met Cys Leu Phe His Leu Thr His Leu Ser
 835 840 845
 Asp Ile Gly Glu Gly Met Asp Tyr Ile Val Lys Ser Leu Ser Ser Glu
 850 855 860
 Pro Cys Asp Leu Glu Glu Ile Gln Leu Val Ser Cys Cys Leu Ser Ala
 865 870 875 880
 Asn Ala Val Lys Ile Leu Ala Gln Asn Leu His Asn Leu Val Lys Leu
 885 890 895
 Ser Ile Leu Asp Leu Ser Glu Asn Tyr Leu Glu Lys Asp Gly Asn Glu
 900 905 910
 Ala Leu His Glu Leu Ile Asp Arg Met Asn Val Leu Glu Gln Leu Thr
 915 920 925
 Ala Leu Met Leu Pro Trp Gly Cys Asp Val Gln Gly Ser Leu Ser Ser
 930 935 940
 Leu Leu Lys His Leu Glu Glu Val Pro Gln Leu Val Lys Leu Gly Leu
 945 950 955 960
 Lys Asn Trp Arg Leu Thr Asp Thr Glu Ile Arg Ile Leu Gly Ala Phe
 965 970 975
 Phe Gly Lys Asn Pro Leu Lys Asn Phe Gln Gln Leu Asn Leu Ala Gly
 980 985 990
 Asn Arg Val Ser Ser Asp Gly Trp Leu Ala Phe Met Gly Val Phe Glu
 995 1000 1005

Asn Leu Lys Gln Leu Val Phe Phe Asp Phe Ser Thr Lys Glu Phe Leu
 1010 1015 1020
 Pro Asp Pro Ala Leu Val Arg Lys Leu Ser Gln Val Leu Ser Lys Leu
 1025 1030 1035 104
 Thr Phe Leu Gln Glu Ala Arg Leu Val Gly Trp Gln Phe Asp Asp Asp
 1045 1050 1055
 Asp Leu Ser Val Ile Thr Gly Ala Phe Lys Leu Val Thr Ala
 1060 1065 1070

<210> 50
 <211> 487
 <212> PRT
 <213> Homo sapiens

<400> 50
 Met Pro Pro Leu Pro Gln Trp Ser Phe Pro Arg Pro Asp His Cys His
 1 5 10 15
 Val Thr Phe Val Thr Leu Lys Cys Asp Ser Ser Lys Lys Arg Arg Arg
 20 25 30
 Gly Arg Lys Ser Pro Ser Lys Glu Val Ser His Ile Thr Ala Glu Phe
 35 40 45
 Glu Ile Glu Thr Lys Met Glu Glu Ala Ser Asp Thr Cys Glu Ala Asp
 50 55 60
 Cys Leu Arg Lys Arg Ala Glu Gln Ser Leu Gln Ala Ala Ile Lys Thr
 65 70 75 80
 Leu Arg Lys Ser Ile Gly Arg Gln Gln Phe Tyr Val Gln Val Ser Gly
 85 90 95
 Thr Glu Tyr Glu Val Ala Gln Arg Pro Ala Lys Ala Leu Glu Gly Gln
 100 105 110
 Gly Ala Cys Gly Ala Gly Gln Val Leu Gln Asp Ser Lys Cys Val Ala
 115 120 125
 Cys Gly Pro Gly Thr His Phe Gly Gly Glu Leu Gly Gln Cys Val Ser
 130 135 140
 Cys Met Pro Gly Thr Tyr Gln Asp Met Glu Gly Gln Leu Ser Cys Thr
 145 150 155 160
 Pro Cys Pro Ser Ser Asp Gly Leu Gly Leu Pro Gly Ala Arg Asn Val
 165 170 175
 Ser Glu Cys Gly Gly Lys Cys Gly Pro Arg Arg Arg Gly Phe Phe Ser
 180 185 190
 Ala Asp Gly Phe Lys Pro Cys Gln Ala Cys Pro Val Gly Thr Tyr Gln
 195 200 205
 Pro Glu Pro Gly Arg Thr Gly Cys Phe Pro Cys Gly Gly Gly Leu Leu

```

      210              215              220
Thr Lys His Glu Gly Thr Thr Ser Phe Gln Asp Cys Glu Ala Lys Val
225              230              235              240
His Cys Ser Pro Gly His His Tyr Asn Thr Thr Thr His Arg Cys Ile
      245              250              255
Arg Cys Pro Val Gly Thr Tyr Gln Pro Glu Phe Gly Gln Asn His Cys
      260              265              270
Ile Thr Cys Pro Gly Asn Thr Ser Thr Asp Phe Asp Gly Ser Thr Asn
      275              280              285
Val Thr His Cys Lys Asn Gln His Cys Gly Gly Glu Leu Gly Asp Tyr
      290              295              300
Thr Gly Tyr Ile Glu Ser Pro Asn Tyr Pro Gly Asp Tyr Pro Ala Asn
305              310              315              320
Ala Glu Cys Val Trp His Ile Ala Pro Pro Pro Lys Arg Arg Ile Leu
      325              330              335
Ile Val Val Pro Glu Ile Phe Leu Pro Ile Glu Asp Glu Cys Gly Asp
      340              345              350
Val Leu Val Met Arg Lys Ser Ala Ser Pro Thr Ser Ile Thr Thr Tyr
      355              360              365
Glu Thr Cys Gln Thr Tyr Glu Arg Pro Ile Ala Phe Thr Ser Arg Ser
      370              375              380
Arg Lys Leu Trp Ile Gln Phe Lys Ser Asn Glu Gly Asn Ser Gly Lys
385              390              395              400
Gly Phe Gln Val Pro Tyr Val Thr Tyr Asp Glu Asp Tyr Gln Gln Leu
      405              410              415
Ile Glu Asp Ile Val Arg Asp Gly Arg Leu Tyr Ala Ser Glu Asn His
      420              425              430
Gln Glu Ile Leu Lys Asp Lys Lys Leu Ile Lys Ala Leu Phe Asp Val
      435              440              445
Leu Ala His Pro Gln Asn Tyr Phe Lys Tyr Thr Ala Gln Glu Ser Lys
      450              455              460
Glu Met Phe Pro Arg Ser Phe Ile Lys Leu Leu Arg Ser Lys Val Ser
465              470              475              480
Arg Phe Leu Arg Pro Tyr Lys
      485

```

<210> 51

<211> 965

<212> PRT

<213> Homo sapiens

<400> 51

Met	Gly	Ala	Ala	Ala	Val	Arg	Trp	His	Leu	Cys	Val	Leu	Leu	Ala	Leu
1				5					10					15	
Gly	Thr	Arg	Gly	Arg	Leu	Ala	Gly	Gly	Ser	Gly	Leu	Pro	Gly	Ser	Val
			20					25					30		
Asp	Val	Asp	Glu	Cys	Ser	Glu	Gly	Thr	Asp	Asp	Cys	His	Ile	Asp	Ala
			35				40					45			
Ile	Cys	Gln	Asn	Thr	Pro	Lys	Ser	Tyr	Lys	Cys	Leu	Cys	Lys	Pro	Gly
	50					55					60				
Tyr	Lys	Gly	Glu	Gly	Lys	Gln	Cys	Glu	Asp	Ile	Asp	Glu	Cys	Glu	Asn
65					70					75				80	
Asp	Tyr	Tyr	Asn	Gly	Gly	Cys	Val	His	Glu	Cys	Ile	Asn	Ile	Pro	Gly
			85					90					95		
Asn	Tyr	Arg	Cys	Thr	Cys	Phe	Asp	Gly	Phe	Met	Leu	Ala	His	Asp	Gly
			100					105					110		
His	Asn	Cys	Leu	Asp	Val	Asp	Glu	Cys	Gln	Asp	Asn	Asn	Gly	Gly	Cys
			115				120					125			
Gln	Gln	Ile	Cys	Val	Asn	Ala	Met	Gly	Ser	Tyr	Glu	Cys	Gln	Cys	His
	130					135					140				
Ser	Gly	Phe	Phe	Leu	Ser	Asp	Asn	Gln	His	Thr	Cys	Ile	His	Arg	Ser
145					150					155				160	
Asn	Glu	Gly	Met	Asn	Cys	Met	Asn	Lys	Asp	His	Gly	Cys	Ala	His	Ile
			165					170				175			
Cys	Arg	Glu	Thr	Pro	Lys	Gly	Gly	Val	Ala	Cys	Asp	Cys	Arg	Pro	Gly
			180					185				190			
Phe	Asp	Leu	Ala	Gln	Asn	Gln	Lys	Asp	Cys	Thr	Leu	Thr	Cys	Asn	Tyr
		195					200					205			
Gly	Asn	Gly	Gly	Cys	Gln	His	Ser	Cys	Glu	Asp	Thr	Asp	Thr	Gly	Pro
	210					215					220				
Thr	Cys	Gly	Cys	His	Gln	Lys	Tyr	Ala	Leu	His	Ser	Asp	Gly	Arg	Thr
225					230					235				240	
Cys	Ile	Glu	Thr	Cys	Ala	Val	Asn	Asn	Gly	Gly	Cys	Asp	Arg	Thr	Cys
			245					250				255			
Lys	Asp	Thr	Ala	Thr	Gly	Val	Arg	Cys	Ser	Cys	Pro	Val	Gly	Phe	Thr
			260					265				270			
Leu	Gln	Pro	Asp	Gly	Lys	Thr	Cys	Lys	Asp	Ile	Asn	Glu	Cys	Leu	Val
		275					280					285			
Asn	Asn	Gly	Gly	Cys	Asp	His	Phe	Cys	Arg	Asn	Thr	Val	Gly	Ser	Phe
	290					295					300				
Glu	Cys	Gly	Cys	Arg	Lys	Gly	Tyr	Lys	Leu	Leu	Thr	Asp	Glu	Arg	Thr
305					310					315				320	
Cys	Gln	Asp	Ile	Asp	Glu	Cys	Ser	Phe	Glu	Arg	Thr	Cys	Asp	His	Ile
			325					330				335			

Cys Ile Asn Ser Pro Gly Ser Phe Gln Cys Leu Cys His Arg Gly Tyr
 340 345 350
 Ile Leu Tyr Gly Thr Thr His Cys Gly Asp Val Asp Glu Cys Ser Met
 355 360 365
 Ser Asn Gly Ser Cys Asp Gln Gly Cys Val Asn Thr Lys Gly Ser Tyr
 370 375 380
 Glu Cys Val Cys Pro Pro Gly Arg Arg Leu His Trp Asn Gly Lys Asp
 385 390 395 400
 Cys Val Glu Thr Gly Lys Cys Leu Ser Arg Ala Lys Thr Ser Pro Arg
 405 410 415
 Ala Gln Leu Ser Cys Ser Lys Ala Gly Gly Val Glu Ser Cys Phe Leu
 420 425 430
 Ser Cys Pro Ala His Thr Leu Phe Val Pro Asp Ser Glu Asn Ser Tyr
 435 440 445
 Val Leu Ser Cys Gly Val Pro Gly Pro Gln Gly Lys Ala Leu Gln Lys
 450 455 460
 Arg Asn Gly Thr Ser Ser Gly Leu Gly Pro Ser Cys Ser Asp Ala Pro
 465 470 475 480
 Thr Thr Pro Ile Lys Gln Lys Ala Arg Phe Lys Ile Arg Asp Ala Lys
 485 490 495
 Cys His Leu Arg Pro His Ser Gln Ala Arg Ala Lys Glu Thr Ala Arg
 500 505 510
 Gln Pro Leu Leu Asp His Cys His Val Thr Phe Val Thr Leu Lys Cys
 515 520 525
 Asp Ser Ser Lys Lys Arg Arg Arg Gly Arg Lys Ser Pro Ser Lys Glu
 530 535 540
 Val Ser His Ile Thr Ala Glu Phe Glu Ile Glu Thr Lys Met Glu Glu
 545 550 555 560
 Ala Ser Asp Thr Cys Glu Ala Asp Cys Leu Arg Lys Arg Ala Glu Gln
 565 570 575
 Ser Leu Gln Ala Ala Ile Lys Thr Leu Arg Lys Ser Ile Gly Arg Gln
 580 585 590
 Gln Phe Tyr Val Gln Val Ser Gly Thr Glu Tyr Glu Val Ala Gln Arg
 595 600 605
 Pro Ala Lys Ala Leu Glu Gly Gln Gly Ala Cys Gly Ala Gly Gln Val
 610 615 620
 Leu Gln Asp Ser Lys Cys Val Ala Cys Gly Pro Gly Thr His Phe Gly
 625 630 635 640
 Gly Glu Leu Gly Gln Cys Val Ser Cys Met Pro Gly Thr Tyr Gln Asp
 645 650 655
 Met Glu Gly Gln Leu Ser Cys Thr Pro Cys Pro Ser Ser Asp Gly Leu
 660 665 670

Gly Leu Pro Gly Ala Arg Asn Val Ser Glu Cys Gly Gly Gln Cys Ser
 675 680 685
 Pro Gly Phe Phe Ser Ala Asp Gly Phe Lys Pro Cys Gln Ala Cys Pro
 690 695 700
 Val Gly Thr Tyr Gln Pro Glu Pro Gly Arg Thr Gly Cys Phe Pro Cys
 705 710 715 720
 Gly Gly Gly Leu Leu Thr Lys His Glu Gly Thr Thr Ser Phe Gln Asp
 725 730 735
 Cys Glu Ala Lys Val His Cys Ser Pro Gly His His Tyr Asn Thr Thr
 740 745 750
 Thr His Arg Cys Ile Arg Cys Pro Val Gly Thr Tyr Gln Pro Glu Phe
 755 760 765
 Gly Gln Asn His Cys Ile Thr Cys Pro Gly Asn Thr Ser Thr Asp Phe
 770 775 780
 Asp Gly Ser Thr Asn Val Thr His Cys Lys Asn Gln His Cys Gly Gly
 785 790 795 800
 Glu Leu Gly Asp Tyr Thr Gly Tyr Ile Glu Ser Pro Asn Tyr Pro Gly
 805 810 815
 Asp Tyr Pro Ala Asn Ala Glu Cys Val Trp His Ile Ala Pro Pro Pro
 820 825 830
 Lys Arg Arg Ile Leu Ile Val Val Pro Glu Ile Phe Leu Pro Ile Glu
 835 840 845
 Asp Glu Cys Gly Asp Val Leu Val Met Arg Lys Ser Ala Ser Pro Thr
 850 855 860
 Ser Ile Thr Thr Tyr Glu Thr Cys Gln Thr Tyr Glu Arg Pro Ile Ala
 865 870 875 880
 Phe Thr Ser Arg Ser Arg Lys Leu Trp Ile Gln Phe Lys Ser Asn Glu
 885 890 895
 Gly Asn Ser Gly Lys Gly Phe Gln Val Pro Tyr Val Thr Tyr Asp Gly
 900 905 910
 Lys Ile His Cys Leu His Gly Pro Leu Cys Thr Ala Gln Ala Gly Pro
 915 920 925
 Trp Arg His Arg Asp Glu Ser His Val Pro Ala Pro Ser Gly Ser Cys
 930 935 940
 Asp Leu Ala Gly Thr Asp Leu Glu Ala Glu Arg Thr Leu Ser Gly Ala
 945 950 955 960
 Arg Ala Arg Gln Ala
 965

<210> 52

<211> 716

<212> PRT

<213> Homo sapiens

<400> 52

```

Met Ala Arg Met Ser Phe Val Ile Ala Ala Cys Gln Leu Val Leu Gly
 1              5              10              15
Leu Leu Met Thr Ser Leu Thr Glu Ser Ser Ile Gln Asn Ser Glu Cys
      20              25              30
Pro Gln Leu Cys Val Cys Glu Ile Arg Pro Trp Phe Thr Pro Gln Ser
      35              40              45
Thr Tyr Arg Glu Ala Thr Thr Val Asp Cys Asn Asp Leu Arg Leu Thr
      50              55              60
Arg Ile Pro Ser Asn Leu Ser Ser Asp Thr Gln Val Leu Leu Leu Gln
      65              70              75              80
Ser Asn Asn Ile Ala Lys Thr Val Asp Glu Leu Gln Gln Leu Phe Asn
      85              90              95
Leu Thr Glu Leu Asp Phe Ser Gln Asn Asn Phe Thr Asn Ile Lys Glu
      100             105             110
Val Gly Leu Ala Asn Leu Thr Gln Leu Thr Thr Leu His Leu Glu Glu
      115             120             125
Asn Gln Ile Thr Glu Met Thr Asp Tyr Cys Leu Gln Asp Leu Ser Asn
      130             135             140
Leu Gln Glu Leu Tyr Ile Asn His Asn Gln Ile Ser Thr Ile Ser Ala
      145             150             155             160
His Ala Phe Ala Gly Leu Lys Asn Leu Leu Arg Leu His Leu Asn Ser
      165             170             175
Asn Lys Leu Lys Val Ile Asp Ser Arg Trp Phe Asp Ser Thr Pro Asn
      180             185             190
Leu Glu Ile Leu Met Ile Gly Glu Asn Pro Val Ile Gly Ile Leu Asp
      195             200             205
Met Asn Phe Lys Pro Leu Ala Asn Leu Arg Ser Leu Val Leu Ala Gly
      210             215             220
Met Tyr Leu Thr Asp Ile Pro Gly Asn Ala Leu Val Gly Leu Asp Ser
      225             230             235             240
Leu Glu Ser Leu Ser Phe Tyr Asp Asn Lys Leu Val Lys Val Pro Gln
      245             250             255
Leu Ala Leu Gln Lys Val Pro Asn Leu Lys Phe Leu Asp Leu Asn Lys
      260             265             270
Asn Pro Ile His Lys Ile Gln Glu Gly Asp Phe Lys Asn Met Leu Arg
      275             280             285
Leu Lys Glu Leu Gly Ile Asn Asn Met Gly Glu Leu Val Ser Val Asp
      290             295             300
Arg Tyr Ala Leu Asp Asn Leu Pro Glu Leu Thr Lys Leu Glu Ala Thr

```

305		310		315		320
Asn Asn Pro Lys Leu Ser Tyr Ile His Arg Leu Ala Phe Arg Ser Val						
	325		330		335	
Pro Ala Leu Glu Ser Leu Met Leu Asn Asn Asn Ala Leu Asn Ala Ile						
	340		345		350	
Tyr Gln Lys Thr Val Glu Ser Leu Pro Asn Leu Arg Glu Ile Ser Ile						
	355		360		365	
His Ser Asn Pro Leu Arg Cys Asp Cys Val Ile His Trp Ile Asn Ser						
	370		375		380	
Asn Lys Thr Asn Ile Arg Phe Met Glu Pro Leu Ser Met Phe Cys Ala						
385		390		395		400
Met Pro Pro Glu Tyr Lys Gly His Gln Val Lys Glu Val Leu Ile Gln						
	405		410		415	
Asp Ser Ser Glu Gln Cys Leu Pro Met Ile Ser His Asp Ser Phe Pro						
	420		425		430	
Asn Arg Leu Asn Val Asp Ile Gly Thr Thr Val Phe Leu Asp Cys Arg						
	435		440		445	
Ala Met Ala Glu Pro Glu Pro Glu Ile Tyr Trp Val Thr Pro Ile Gly						
	450		455		460	
Asn Lys Ile Thr Val Glu Thr Leu Ser Asp Lys Tyr Lys Leu Ser Ser						
465		470		475		480
Glu Gly Thr Leu Glu Ile Ser Asn Ile Gln Ile Glu Asp Ser Gly Arg						
	485		490		495	
Tyr Thr Cys Val Ala Gln Asn Val Gln Gly Ala Asp Thr Arg Val Ala						
	500		505		510	
Thr Ile Lys Val Asn Gly Thr Leu Leu Asp Gly Thr Gln Val Leu Lys						
	515		520		525	
Ile Tyr Val Lys Gln Thr Glu Ser His Ser Ile Leu Val Ser Trp Lys						
	530		535		540	
Val Asn Ser Asn Val Met Thr Ser Asn Leu Lys Trp Ser Ser Ala Thr						
545		550		555		560
Met Lys Ile Asp Asn Pro His Ile Thr Tyr Thr Ala Arg Val Pro Val						
	565		570		575	
Asp Val His Glu Tyr Asn Leu Thr His Leu Gln Pro Ser Thr Asp Tyr						
	580		585		590	
Glu Val Cys Leu Thr Val Ser Asn Ile His Gln Gln Thr Gln Lys Ser						
	595		600		605	
Cys Val Asn Val Thr Thr Lys Asn Ala Ala Phe Ala Val Asp Ile Ser						
	610		615		620	
Asp Gln Glu Thr Ser Thr Ala Leu Ala Ala Val Met Gly Ser Met Phe						
625		630		635		640
Ala Val Ile Ser Leu Ala Ser Ile Ala Val Tyr Phe Ala Lys Arg Phe						

				645					650					655			
Lys	Arg	Lys	Asn	Tyr	His	His	Ser	Leu	Lys	Lys	Tyr	Met	Gln	Lys	Thr		
			660						665					670			
Ser	Ser	Ile	Pro	Leu	Asn	Glu	Leu	Tyr	Pro	Pro	Leu	Ile	Asn	Leu	Trp		
			675						680					685			
Glu	Gly	Asp	Ser	Glu	Lys	Asp	Lys	Asp	Gly	Ser	Ala	Asp	Thr	Lys	Pro		
			690						695					700			
Thr	Gln	Val	Asp	Thr	Ser	Arg	Ser	Tyr	Tyr	Met	Trp						
705						710					715						

